CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218347Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 25, 2024
Application Type and Number:	NDA 218347
Product Name and Strength:	Rinvoq LQ (upadacitinib) oral solution, 1 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Abbvie Inc (Abbvie)
PNR ID #:	2024-1044725674
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader (Acting):	Damon Birkemeier, PharmD, FISMP, NREMT
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Rinvoq LQ, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Abbvie submitted an external name study, conducted by [redacted] for this proposed proprietary name.

1.1 REGULATORY HISTORY

Abbvie previously submitted the proposed proprietary name, [redacted] *** under NDA 218347 on June 28, 2023. However, on October 25, 2023, we found the name, [redacted] *** unacceptable because the [redacted]

Abbvie previously submitted the proposed proprietary name, [redacted] ***, under NDA 218347 on December 21, 2023. On March 11, 2024, we notified Abbvie of our preliminary concerns with their proposed proprietary name, [redacted] ***, and provided Abbvie with regulatory options to address our concerns via teleconference.[b] Subsequently, on March 12, 2024, Abbvie submitted a withdrawal of request for proprietary name review for [redacted] ***.

Thus, Abbvie submitted the proposed proprietary name, Rinvoq LQ, for review on March 12, 2024 under NDA 218347.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on March 12, 2024.

Table 1. Relevant Product Information for Rinvoq LQ and Rinvoq

Product Name	Rinvoq LQ	Rinvoq[c]
Intended Pronunciation	RIN-voke EL-CUE	RIN-voke
Application Type and #	NDA 218347	NDA 211675
Initial Approval Date	N/A	August 16, 2019

[a] McMillan, T. Proprietary Name Review for [redacted]). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 OCT 25. PNR ID No. 2023-1044725216.

[b] Mathew, D. Memorandum of Teleconference for upadacitinib (NDA 218347). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US): 2024 MAR 11. Available from: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af80730a78.

[c] Proposed Prescribing Information for Rinvoq NDA 211675/S-021. Available from: \\CDSESUB1\evsprod\NDA211675\0288\m1\us\114-labeling\draft\labeling\uspi-upadacitinib-tablet-and-os.docx

Active Ingredient	upadacitinib	
Indication	Polyarticular Juvenile Idiopathic Arthritis: Patients 2 years of age and older with active polyarticular (b) (4) juvenile idiopathic arthritis (b) (4) who have had an inadequate response or intolerance to one or more TNF blockers.	Rheumatoid Arthritis: Adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers. Psoriatic Arthritis: Adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers. Atopic Dermatitis: Adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable. Ulcerative Colitis: Adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers. Crohn's Disease: Adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers. Ankylosing Spondylitis: Adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers. Non-radiographic Axial Spondyloarthritis: Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy.

<table>
<tr><td></td><td></td><td><u>Polyarticular Juvenile Idiopathic Arthritis:</u> Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.</td></tr>
<tr><td>Route of Administration</td><td colspan="2">oral</td></tr>
<tr><td>Dosage Form</td><td>solution</td><td>extended-release tablets</td></tr>
<tr><td>Strength</td><td>1 mg/mL</td><td>15 mg, 30 mg, and 45 mg</td></tr>
<tr><td>Dose and Frequency</td><td>The recommended dose is based on body weight:
<table>
<tr><th>Patient weight (2 years of age and older)</th><th>Dosing Regimen</th></tr>
<tr><td>10 to < 20 kg</td><td>3 mg (3 mL oral solution) twice daily</td></tr>
<tr><td>20 to < 30 kg</td><td>4 mg (4 mL oral solution) twice daily</td></tr>
<tr><td>≥ 30 kg</td><td>6 mg (6 mL oral solution) twice daily</td></tr>
</table>
RINVOQ LQ oral solution is not substitutable with RINVOQ extended release tablets. Changes between RINVOQ LQ oral solution and RINVOQ extended-release tablets should be made by the health care provider.</td><td><u>Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Nonradiographic Axial Spondyloarthritis</u>
• The recommended dosage is 15 mg once daily.
<u>Atopic Dermatitis</u>
• Pediatric Patients 12 Years of Age and Older Weighing at Least 40 kg and
• Adults Less Than 65 Years of Age: Initiate treatment with 15 mg orally once daily. If an adequate response is not achieved, consider increasing the dosage to 30 mg orally once daily.
• Adults 65 Years of Age and Older: Recommended dosage is 15 mg once daily.
• Severe Renal Impairment: Recommended dosage is 15 mg once daily.
<u>Ulcerative Colitis</u>
• Adults: The recommended induction dosage is 45 mg once daily for 8 weeks. The recommended maintenance dosage is 15 mg once daily. A maintenance dosage of 30 mg once daily may be considered for</td></tr>
</table>

patients with refractory, severe, or extensive disease. Discontinue RINVOQ if adequate therapeutic response is not achieved with the 30 mg dosage. Use the lowest effective dosage needed to maintain response.

Crohn's Disease

• Adults: The recommended induction dosage is 45 mg once daily for 12 weeks. The recommended maintenance dosage is 15 mg once daily. A maintenance dosage of 30 mg once daily may be considered for patients with refractory, severe, or extensive disease. Discontinue RINVOQ if an adequate therapeutic response is not achieved with the 30 mg dosage. Use the lowest effective dosage needed to maintain response.

Polyarticular (b) (4) juvenile idiopathic arthritis (b) (4):

Patient weight (2 years of age and older)	Dosing Regimen
10 to < 20 kg	Not Recommended
20 to < 30 kg	Not Recommended
≥30 kg	15 mg (one 15 mg tablet) once daily
RINVOQ extended-release tablets is not substitutable with RINVOQ LQ oral solution. Changes between RINVOQ extended-release tablets and RINVOQ LQ oral solution should be made by the health care provider.	

How Supplied	This product will be supplied as 1 mg/mL oral solution in HDPE bottles. Each bottle contains a labeled volume of 180 mL of solution. The bottle is packaged in a carton with one press-in bottle adapter and one 10 mL oral dosing syringe.	15 mg: 30 tablets in a bottle 30 mg: 30 tablets in a bottle 45 mg: 28 tablets in a bottle
Storage	Store at 2˚C to 25˚C (36˚F to 77˚F). Store in the original bottle in order to protect from moisture.	

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Rinvoq LQ.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Rinvoq LQ would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) concurred with the findings of OPDP's assessment for Rinvoq LQ. The Division of Rheumatology and Transplant Medicine (DRTM) did not comment on the findings of OPDP's assessment for Rinvoq LQ.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Rinvoq LQ.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name.[d]

2.2.2 Components of the Proposed Proprietary Name

Abbvie indicated in their submission that the proposed proprietary name, Rinvoq LQ, was *"loosely derived from a combination of letters that are intended to represent immediate-release oral solution".* The proposed proprietary name, Rinvoq LQ, is comprised of a root name and a modifier "LQ".

2.2.3 Comments from Other Review Disciplines at Initial Review

On March 21, 2024, the Division of Rheumatology and Transplant Medicine (DRTM) did not forward any comments or concerns relating to Rinvoq LQ at the initial phase of the review but noted Serostim LQ as a proprietary name using the modifier, "LQ". See Section 2.2.5 for full evaluation of the modifier.

[d] USAN stem search conducted on March 12, 2024.

2.2.4 FDA Name Simulation Studies

Seventy-seven (n=77) practitioners participated in DMEPA's prescription studies for Rinvoq LQ. Two CPOE participants responded with only the root name "Rinvoq", and one voice participant responded with a misinterpretation of the root name ("Remvok"), without the modifier. Furthermore, one outpatient participant misinterpreted the modifier as "LA", which is a known modifier indicating long-acting formulation. See section 2.2.5 for the full evaluation of the modifier.

Appendix B contains the results from the rest of the prescription simulation studies where the responses did not sound nor look similar to any currently marketed products or any products in the pipeline.

2.2.5 Safety Analysis of the Proposed Modifier, "LQ"

The proposed proprietary name, Rinvoq LQ, is comprised of the root name, "Rinvoq" and the modifier "LQ". Abbvie proposes the modifier "LQ" to differentiate the proposed oral solution from the currently marketed product, Rinvoq, which is an extended-release tablet. As such, we evaluated the following: (1) evaluation of the use of the same root name, (2) use of a modifier to differentiate the product, and 3) evaluation of the proposed modifier, LQ.

1. Evaluation of the use of the same root name "Rinvoq"

   Rinvoq has been marketed as the proprietary name for upadacitinib since approval on August 16, 2019. We note that Rinvoq and Rinvoq LQ have the same active ingredient (upadacitinib), route of administration (oral), and share the indication for polyarticular (b) (4) juvenile idiopathic arthritis (b) (4); however, the dosage form (tablet vs. oral solution), strength(s) (15 mg, 30 mg, and 45 mg vs. 1 mg/mL), and recommended dosage(s) differ (15 mg, 30 mg, or 45 mg once daily vs. 3 mg, 4 mg, or 6 mg twice daily depending on patient weight). We note that Rinvoq has additional indications for which Rinvoq LQ is not indicated for. See Table 1 for a comparison of product characteristics. Our routine postmarketing surveillance has not identified name confusion medication errors associated with the root name.

2. Evaluation of the use of a modifier to differentiate the product

   Abbvie proposes to differentiate the proposed product, Rinvoq LQ, from the currently marketed extended-release tablet formulation, Rinvoq, using the modifier "LQ" in the proposed proprietary name nomenclature. Rinvoq LQ is an oral solution and the use of a modifier may help to distinguish it from Rinvoq extended-release tablets. The use of a modifier to differentiate product characteristics between products, such as a different dosage form, is a common naming practice as part of a family brand. As stated above, Rinvoq and Rinvoq LQ share the indication of (b) (4) However, Rinvoq extended-release tablets is not recommended for pediatric patients aged 2 years and older and weighing less than 30 kg (see Table 1).

In our evaluation, we considered the risk of name confusion if the modifier is omitted or overlooked. We note that omission and oversight of modifiers is cited in literature as a common cause of medication errors.[e] Postmarket experience shows that family branding may result in medication errors if the modifier is omitted, and the product characteristics are similar or overlap. As noted in Table 1 above, the strengths (1 mg/mL vs. 15 mg, 30 mg, 45 mg), dosage form (oral solution vs. extended-release tablets), and dose/frequency (3 mg (3 mL), 4 mg (4 mL), or 6 mg (6 mL) twice daily vs. 15 mg, 30 mg, 45 mg once daily) differ between the products. Therefore, if the modifier "LQ" is omitted or overlooked, and a prescription or medication order for "Rinvoq LQ 3 mg [4 mg or 6 mg] twice daily" is interpreted as "Rinvoq 3 mg [4 mg or 6 mg] twice daily" the pharmacist would need to contact the prescriber to verify the dose as Rinvoq extended-release tablets are not available in such strengths as proposed for Rinvoq LQ.

It is important to note that Rinvoq extended-release tablets is not substitutable with Rinvoq LQ oral solution and the formulations are not equivalent on a milligram-to-milligram basis. Patients with (b) (4) weighing 30 kg or more can take either the extended-release tablet formulation at a dose of 15 mg (one 15 mg tablet) once daily or the proposed oral solution at a dose of 6 mg (6 mL) twice daily. We evaluated the risk of dosing errors should the two formulations be confused (i.e., a pediatric patient intended to receive Rinvoq 15 mg once daily but receives Rinvoq LQ 15 mg (15 mL) once daily), in the context of the naming strategy using a modifier. However, we note that the differences in product characteristics, in addition to labels/labeling strategies, may provide an added measure of safety.

An alternative to using a modifier to distinguish this product from the currently marketed products is to use a different root name. However, marketing the new product under a unique proprietary name also carries a risk of medication errors, such as therapeutic duplication and overdoses. Although the proposed naming strategy is not devoid of risk because modifiers may be omitted or overlooked, in this case, based on the totality of this information, we do not object to the use of a modifier for this product.

3. Evaluation of the proposed modifier "LQ"

Abbvie indicated that the modifier LQ is *"derived from a combination of letters that are intended to represent immediate-release oral solution".* However, Abbvie did not provide any data in support of the use of the modifier. We note that the name Serostim LQ is on the Institute of Safe Medication Practices' (ISMP) List of Products with Drug Name Suffixes and the meaning provided is "liquid". Additionally, we note that the following currently marketed product has the "LQ" modifier: Hetlioz LQ, which is a prescription oral suspension product. Additionally, we note that we have not identified any postmarketing cases of name confusion associated with the modifier "LQ". We also

[e] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

note that the modifier is not misleading since its intended meaning is "liquid" and Rinvoq LQ is a liquid. Furthermore, if the modifier was misinterpreted as "LA" or long-acting (see results of FDA Prescription Simulation study), it is unlikely that a wrong formulation (i.e., extended-release tablet formulation) would be dispensed due to differences in strength, dose, and frequency. If the modifier was misinterpreted as "SQ" or subcutaneous, for instance, it is unlikely that the product would be administered subcutaneously because it is an oral solution and the proposed labeling and packaging (press-in bottle adaptor, 10 mL oral dosing syringe) do not support a subcutaneous route of administration. Thus, considering the totality of information, we do not object to the use of the modifier "LQ" for this product.

In summary, we find the use of the proposed naming strategy (the use of the same root name, Rinvoq, with a distinguishing modifier) acceptable. Additionally, we find the proposed modifier, "LQ", sufficiently differentiates the proposed product from the currently marketed Rinvoq product. Therefore, based on the totality of information considered above, we do not object to the proposed name, Rinvoq LQ, for the proposed product.

2.2.6 Medication Error Data Selection of Cases

On January 26, 2024, we searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving *Rinvoq* that would be relevant for this review.

Table 2. FAERS Search Strategy

FAERS Field	Search Terms
Initial FDA Receive Dates	No limit
Product Name	Rinvoq
Event	DMEPA Official PNR Name Confusion Search Terms
Country (derived)	USA

The search did not find any cases relevant to this review.

2.2.7 Communication of DMEPA's Determination

On March 25, 2024, DMEPA 1 communicated our determination to the Division of Rheumatology and Transplant Medicine (DRTM).

3 CONCLUSION

The proposed proprietary name, Rinvoq LQ, is conditionally acceptable.

If you have further questions or need clarifications, please contact Davis Mathew, OSE project manager, at 240-402-4559.

3.1 COMMENTS TO ABBVIE INC

We have completed our review of the proposed proprietary name, Rinvoq LQ, and have concluded that this proprietary name is conditionally acceptable.

4 REFERENCES

1. *USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)*

   USAN Stems List contains all the recognized USAN stems.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. Misbranding Assessment: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. Safety Assessment: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.[f]

*Table 2- Prescreening Checklist for Proposed Proprietary Name

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	Is the proposed name obviously similar in spelling and pronunciation to other names?
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	Are there inert or inactive ingredients referenced in the proprietary name?
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).

[f] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

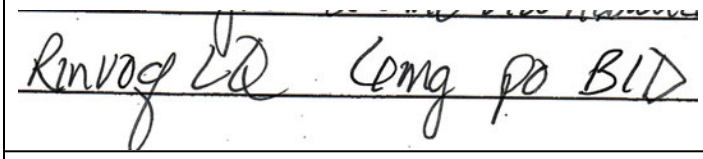
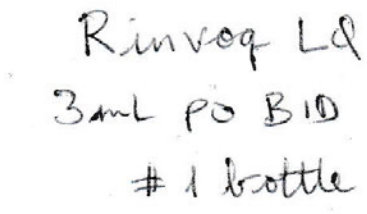
Y/N	Does the proprietary name include combinations of active ingredients?
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	Is there a United States Adopted Name (USAN) stem in the proprietary name?
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	Is this proprietary name used for another product that does not share at least one common active ingredient?
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	Is this a proprietary name of a discontinued product?
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Rinvoq LQ Study (Conducted on February 23, 2024)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Rinvoq LQ 3 mL PO BID Disp: 1 Bottle
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Rinvoq LQ	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Rinvoq LQ - 2024-02-23
People Received Study: 164
People Responded: 77

Total	19	24	12	22	77
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
BRINVOKE LQ	0	0	1	0	1
GRINVOKE LQ	0	0	1	0	1
REMVOK	0	0	1	0	1
RENVOK LQ	0	0	1	0	1
RENVOKE LQ	0	0	1	0	1
RENVOQ LQ	0	0	2	0	2
RIMVOQLQ	0	0	1	0	1
RINVOQ	0	0	0	2	2

RINVOQ LA	0	1	0	0	1
RINVOQ LQ	19	23	3	20	65
RINVOQUE LQ	0	0	1	0	1

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/

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