



NDA 211675/S-021  
NDA 211675/S-022

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING  
REQUIREMENT(S)  
RELEASE FROM POSTMARKETING  
REQUIREMENT**

AbbVie Inc.  
Attention: Leilane Oshiro Gaglianone  
Senior Manager, Regulatory Affairs  
1 N. Waukegan Road  
Dept. PA72, Bldg. AP30-4  
North Chicago, IL 60064

Dear Leilane Oshiro Gaglianone:

Please refer to your supplemental new drug application (sNDA) 211675/S-021 received June 28, 2023, and sNDA 211675/S-022 received June 30, 2023, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rinvoq (upadacitinib) extended-release tablets.

These Prior Approval supplemental NDAs 211675/S-021 and 211675/S-022 provide for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one of more tumor necrosis factor (TNF) blockers, and the treatment of patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, respectively.

**APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (Prescribing Information and Medication Guide), with the addition of any labeling changes in pending

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

“Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 211675/S-021 and NDA 211675/S-022.**” Approval of this submission by FDA is not required before the labeling is used.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

## **FULFILLMENT OF POSTMARKETING REQUIREMENTS**

We have received your submissions dated June 28, 2023, and June 30, 2023, containing the final reports for the following postmarketing requirements listed in the August 16, 2019, and December 14, 2021, approval letters.

- 3680-1: Conduct a multiple-dose pharmacokinetic study in children from 2 to less than 18 years of age with juvenile idiopathic arthritis (JIA).
- 4201-1 Provide PK and safety information to support the pediatric assessment of upadacitinib for the treatment of juvenile psoriatic arthritis (jPsA) in children 5 to 17 years of age.

We have reviewed your submissions and conclude that the above requirements are fulfilled.

In addition, we have received your submission dated March 11, 2024, containing a request to release the following postmarketing requirement listed in the August 16, 2019, approval letter.

- 3680-2: Conduct a randomized withdrawal, double-blind, placebo-controlled study to evaluate the efficacy and safety of upadacitinib in children from 2 to less than 18 years of age with polyarticular-course JIA.

We have reviewed your submission and conclude that the above requirement is released as it is no longer needed based on the information in NDA 211675/S-021 supporting the efficacy and safety of upadacitinib for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.

This completes all of your postmarketing requirements acknowledged in our August 16, 2019, and December 14, 2021, letters. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 314.81(b)(2)(vii).

## **POSTMARKETING REQUIREMENTS UNDER 505(o)**

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a known serious risk of malignancies, serious infections (including opportunistic infections), thrombosis, and effects on growth.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

- 4615-1 Conduct a long-term registry study in pediatric patients 2 to less than 18 years of age with polyarticular Juvenile Idiopathic Arthritis (pJIA) or Psoriatic Arthritis (PsA) treated with upadacitinib to characterize the risk of malignancies, serious infections (including opportunistic infections), thrombosis, and effects on growth. The registry should enroll upadacitinib-exposed patients and control groups of pediatric pJIA and PsA patients treated with standard-of-care. The applicant should adjudicate the study outcomes. Patients should be followed for 5 years.

The timetable you submitted on April 11, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	01/2025
Final Protocol Submission:	09/2025
Study Completion:	02/2035
Final Report Submission:	02/2036

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.<sup>3</sup>

Submit clinical protocol(s) to your IND 114717 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

**Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to

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<sup>3</sup> See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.  
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>4</sup>

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.<sup>5</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>6</sup>

### **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

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<sup>4</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

## **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Suprat Saely, Regulatory Project Manager, at [suprat.saely@fda.hhs.gov](mailto:suprat.saely@fda.hhs.gov) or 240-402-1604.

Sincerely,

*{See appended electronic signature page}*

Ozlem Belen, MD, MPH  
Deputy Director  
Division of Rheumatology and Transplant Medicine  
Office of Immunology and Inflammation  
Office of New Drugs  
Center for Drug Evaluation and Research

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

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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.**  
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/s/  
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