NDA 215206

NDA APPROVAL

AbbVie Inc.
Attention: Lillian Justus PharmD, RPh
Manager, Regulatory Affairs
5 Giralda Farms
Madison, NJ 07940

Dear Dr. Justus:

Please refer to your new drug application (NDA) dated and received January 28, 2021, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Qulipta (atogepant) tablets.

This NDA provides for the use of Qulipta (atogepant) tablets for the preventive treatment of episodic migraine in adults.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Information) 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.*[2]

The SPL will be accessible via publicly available labeling repositories.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] 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.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on September 23, 2021, except the 10 mg carton labeling submitted on September 27, 2021, 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 215206**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Qulipta shall be 30 months from the date of manufacture when stored at 20°C – 25°C.

ADVISORY COMMITTEE

Your application for Qulipta was not referred to an FDA advisory committee because the clinical trial design was acceptable, the efficacy findings were clear, and the safety profile was acceptable for use in the intended population.

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.

We are waiving the pediatric study requirement for children 0 to 5 years of age because the necessary studies are impossible or highly impracticable. This is because very few children of this age can be definitively diagnosed with migraine and even fewer would be candidates for preventive therapy.

We are deferring the submission of your pediatric studies for children 6 to 17 years of age because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

4152-1 Juvenile animal toxicology study of atogepant in rat.

Study Completion:	09/2021
Final Report Submission:	12/2021

4152-2 A randomized, double-blind, placebo-controlled efficacy and safety study under PREA for the preventive treatment of episodic migraine in children 6 through 17 years of age. This efficacy study must be designed to show superiority of atogepant over placebo and is to be submitted as a special protocol assessment (SPA). A pharmacokinetic evaluation needs to be conducted in children 6 through 11 years of age to determine the appropriate dosing in the efficacy portion of the study in this age group.

Final Protocol Submission:	10/2022
Study Completion:	10/2028
Final Report Submission:	02/2030

4152-3 A study under PREA to evaluate the long-term safety of preventive treatment of episodic migraine in patients 6 through 17 years of age. This study should be a minimum of 1 year in length.

Final Protocol Submission:	10/2022
Study Completion:	11/2029
Final Report Submission:	02/2030

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.[3]

Submit the protocol(s) to your IND 114780, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

[3] 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.

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 identify an unexpected serious risk of carcinogenicity resulting from the use of Qulipta, or to identify an unexpected serious risk of adverse maternal, fetal, and infant outcomes resulting from the use of Qulipta during pregnancy.

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:

4152-4 A dose-range finding study of orally administered atogepant in female CD-1 mouse.

The timetable you submitted on September 24, 2021, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	05/2022
Final Protocol Submission:	09/2022
Study Completion:	11/2022
Final Report Submission:	04/2023

4152-5 A 2-year carcinogenicity study of orally administered atogepant in female mouse.

The timetable you submitted on September 24, 2021, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	06/2023
Final Protocol Submission:	10/2023
Study Completion:	10/2025
Final Report Submission:	10/2026

4152-6 Prospective pregnancy exposure registry cohort analyses in the United States that compare the maternal, fetal, and infant outcomes of women with migraine exposed to atogepant during pregnancy with two unexposed

control populations: one consisting of women with migraine who have not been exposed to atogepant before and during pregnancy and the other consisting of women without migraine. The registry will identify and record pregnancy complications, major and minor congenital malformations, spontaneous abortions, stillbirths, elective terminations, preterm births, small-for-gestational-age births, and any other adverse outcomes, including postnatal growth and development. Outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

The timetable you submitted on August 12, 2021, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	07/2022
Final Protocol Submission:	05/2023
Annual Interim Report Submissions:	02/2024
	02/2025
	02/2026
	02/2027
	02/2028
	02/2029
	02/2030
	02/2031
	02/2032
	02/2033
	02/2034
	02/2035
Study Completion:	02/2036
Final Report Submission:	02/2037

4152-7 A pregnancy outcomes study using a different study design than provided for in PMR 4152-6 (for example, a retrospective cohort study using claims or electronic medical record data with outcome validation or a case control study) to assess major congenital malformations, spontaneous abortions, stillbirths, preterm births, and small-for-gestational-age births in women exposed to atogepant during pregnancy compared to an unexposed control population.

The timetable you submitted on August 12, 2021, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	07/2022
Final Protocol Submission:	05/2023

Annual Interim Report Submissions:	02/2024
	02/2025
	02/2026
	02/2027
	02/2028
	02/2029
Study Completion:	02/2030
Final Report Submission:	04/2031

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.[4]

Submit clinical protocol(s) to your IND 114780, 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 or FDA's regulations under 21 CFR parts 50 (Protection of Human Subjects) and 56 (Institutional Review Boards).

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 periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B 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 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.

[4] 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.

REQUESTED PHARMACOVIGILANCE

We request that you perform postmarketing surveillance for cardiovascular events, hypertensive events, cerebrovascular events, hepatotoxicity, and serious gastrointestinal events after exposure to Qulipta. Include comprehensive summaries and analyses of these events quarterly as part of your required postmarketing safety reports [e.g., periodic safety update reports (PSUR)]. Include analyses of the events by age and gender. In the analysis of each case, provide an assessment of causality, with documentation of risk factors and results of all assessments that support the diagnosis or the causality, along with extent of exposure to Qulipta and most recent exposure to Qulipta, concomitant therapies, treatment given for the event, and outcome. Include a comparison to background rates expected in a migraine population of the same age and gender.

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.*[5]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

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

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Daniel Ngembus, Regulatory Project Manager, at (301) 837-7345.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Deputy Director
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Information

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/

ERIC P BASTINGS
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