DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 209394

NDA APPROVAL

AbbVie Inc.
Attention: Sejal P. Emerson, PharmD
Director, Regulatory Affairs
1 N. Waukegan Road
Dept. PA77/Bldg. AP30
North Chicago, Illinois 60064

Dear Dr. Emerson:

Please refer to your New Drug Application (NDA) dated and received on December 14, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for MAVYRET™ (glecaprevir and pibrentasvir) tablets, 100 mg/40 mg.

This new drug application provides for the use of MAVYRET™ (glecaprevir and pibrentasvir) tablets for patients with chronic hepatitis C virus (HCV) genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis; and also for patients with HCV GT1 infection who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.

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 text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and text for patient package insert). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 209394**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for glecaprevir and pibrentasvir was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues that were unexpected for the drug classes contained in MAVYRET™ and there were no controversial issues that would benefit from advisory committee discussion.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages from birth to less than 3 years of age years because necessary studies are impossible or highly impracticable. This is because there is a high rate of spontaneous viral clearance and lack of significant disease progression in children less than 3 years of age, therefore, the number of patients requiring treatments is very small.

We are deferring submission of your pediatric study for ages 3 to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. This required study is listed below.

3246-1 Conduct a study to evaluate the pharmacokinetics, safety and treatment response (using sustained virologic response) of glecaprevir and pibrentasvir in pediatric

subjects 3 through less than 18 years of age with chronic hepatitis C virus infection.

Final Protocol Submission:	January, 2017 (submitted)
Study Completion:	July 31, 2022
Final Report Submission:	January 31, 2023

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3246-2 Submit the final SVR_{12} report and datasets, including drug resistance datasets, for the ongoing clinical trial M16-126, evaluating glecaprevir and pibrentasvir in patients with HCV genotype 5 or 6 infection.

The timetable you submitted on July 7, 2017, states that you will conduct this study according to the following schedule:

Trial Completion:	August 1, 2018
Final SVR_{12} Report Submission:	March 31, 2019

3246-3 Submit the final SVR_{12} study report and datasets for the ongoing trial M14-730 (EXPEDITION-2) to provide additional efficacy and safety data in HIV/HCV coinfected subjects receiving glecaprevir and pibrentasvir.

The timetable you submitted on July 7, 2017, states that you will conduct this study according to the following schedule:

Final SVR_{12} Report Submission:	October 31, 2017

3246-4 Conduct a study evaluating the efficacy of glecaprevir and pibrentasvir in HCV genotype 1 infected subjects with prior treatment experience with an NS5A inhibitor plus sofosbuvir regimen.

The timetable you submitted on July 14, 2017, states that you will conduct this study according to the following schedule:

Study Completion:	December 31, 2018
Final SVR_{12} Report Submission:	June 30, 2019

3246-5 Conduct a study to characterize the phenotypic effect of the following individual NS3/4A or NS5A substitutions on the cell culture anti-HCV activity of glecaprevir or pibrentasvir, respectively: genotype 1a NS3_I18V, NS3_N77S, NS3_V116A, NS3_I354V and NS4A_V23A, genotype 3a NS3_I366V, and genotype 1a NS5A_A61T.

The timetable you submitted on July 7, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission:	March 31, 2018

Submit all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert and patient PI to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics 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 Alicia Moruf, PharmD, MPH, Regulatory Project Manager, at (301) 796-3953.

Sincerely,

{See appended electronic signature page}

Edward M. Cox, M.D., M.P.H.
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

EDWARD M COX
08/03/2017