

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207931Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 207931

SUPPL # N/A

HFD # 530/DAVP

Trade Name TECHNIVIE

Generic Name ombitasvir, paritaprevir, ritonavir

Applicant Name AbbVie Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

(b) (4) years

Note: Previously, a 5-year exclusivity for NME NDA 206619 was granted. NDA 206619 contains ombitasvir, paritaprevir, ritonavir, co-packaged with dasabuvir. NDA 207931 also contains ombitasvir and paritaprevir. However, NDA 207931 includes a new indication (treatment of HCV GT4 infection of which Study M13-393 was new and essential for approval).

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21226, 21251, 21906 KALETRA (lopinavir/ritonavir) capsules, oral solution and tablets

NDA# 20659, 20680, 20945, 22417 NORVIR (ritonavir) capsules, tablets and oral solution

NDA# 206619 VIEKIRA PAK (ombitasvir, paritaprevir, ritonavir tablets; dasabuvir tablets, co-packaged for oral use

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

N/A

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

N/A

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

N/A

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1: M13-393: A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Coadministration of ABT-450 with Ritonavir (ABT-450/r) and ABT-267 in Adults with Chronic Hepatitis C Virus Infection (PEARL-I)

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

N/A

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support

the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

N/A

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

M13-393

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 103526 YES !
! NO
! Explain:

Investigation #2
IND # YES !
! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was

not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
!
!
YES ! NO
Explain: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

N/A

=====
Name of person completing form: Elizabeth Thompson
Title: CPMS
Date: June 16, 2015

Name of Office/Division Director signing form: Jeffrey Murray
Title: Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

ELIZABETH G THOMPSON
07/13/2015

JEFFREY S MURRAY
07/13/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹	
NDA # 207931	If NDA, Efficacy Supplement Type: Original <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: TECHNIVIE Established/Proper Name: ombitasvir, paritaprevir, ritonavir Dosage Form: tablets	Applicant: AbbVie Inc. Agent for Applicant (if applicable):
RPM: Elizabeth Thompson	Division: DAVP
NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)	<p><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></p> <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <p><input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check:</p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p>
❖ Actions	
<ul style="list-style-type: none"> Proposed action User Fee Goal Date is <u>August 25, 2015</u> 	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> Previous actions <i>(specify type and date for each action taken)</i> 	<input checked="" type="checkbox"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	<input type="checkbox"/> Received
❖ Application Characteristics ³	

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: Standard Priority
 Chemical classification (new NDAs only): 5
 (confirm chemical classification at time of approval)

- | | |
|--|---|
| <input type="checkbox"/> Fast Track | <input type="checkbox"/> Rx-to-OTC full switch |
| <input type="checkbox"/> Rolling Review | <input type="checkbox"/> Rx-to-OTC partial switch |
| <input type="checkbox"/> Orphan drug designation | <input type="checkbox"/> Direct-to-OTC |
| <input checked="" type="checkbox"/> Breakthrough Therapy designation | |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR
 Submitted in response to a PMC
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input type="checkbox"/> None <input checked="" type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other: Information advisory
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Approval: July 24, 2015
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>) 	<input checked="" type="checkbox"/> Included (7-22-2015)
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<input checked="" type="checkbox"/> Included (2-25-2015)
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>) 	<input checked="" type="checkbox"/> Included (7-22-2015)
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<input checked="" type="checkbox"/> Included (2-25-2015)
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> • Most-recent draft labeling 	<input checked="" type="checkbox"/> Included (7-2-2015)
❖ Proprietary Name	Letters: 3-26-2015 Reviews: 3-23-2015
<ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	
❖ Labeling reviews (<i>indicate dates of reviews</i>)	RPM (PLR format): 4-16-2015 DMEPA: 5-21-2015; 7-24-2015 DMPP/PLT (DRISK): 7-6-2015 (combined review with OPDP for MG) OPDP: 7-7-2015 (PI) SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Product Quality <input checked="" type="checkbox"/> None Other: <input checked="" type="checkbox"/> None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (<i>indicate date of each review</i>)	4/16/2015
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>June 10, 2015</u> If PeRC review not necessary, explain: 	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>)	7-22-2015, 7-21-2015 (2), 7-14-2015 (2), 7-10-2015, 7-1-2015, 6-4-2015, 6-3-2015, 4-17-2015, 4-15-2015, 4-8-2015, 4-6-2015, 4-1-2015, 3-26-2015, 3-16-2015, 3-5-2015, 3-4-2015
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	PeRC minutes: 6-23-2015
❖ Minutes of Meetings	
<ul style="list-style-type: none"> • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) 	October 9, 2014
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> • Mid-cycle Communication (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> • Late-cycle Meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> • Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (<i>indicate dates of mtgs</i>) 	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> • Date(s) of Meeting(s) 	N/A
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	July 22, 2015 *combined DD Summary and CDTL review
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	July 22, 2015 *combined DD Summary and CDTL review
PMR/PMC Development Templates (<i>indicate total number</i>)	3
Clinical	
❖ Clinical Reviews	
<ul style="list-style-type: none"> • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> No separate review
<ul style="list-style-type: none"> • Clinical review(s) (<i>indicate date for each review</i>) 	Filing: 6-17-2015 Primary review: 6-19-2015 (Note: joint clinical, statistics and virology review) 4 month safety update: 7-14-2015
<ul style="list-style-type: none"> • Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None

❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	See primary clinical review dated 6-19-2015
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> N/A
❖ Risk Management <ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	N/A N/A <input checked="" type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	Filing: 4-16-2015 Primary review: 6-19-2015 (Note: joint clinical, statistics and virology review)
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	Filing: 4-24-15 Primary review: 6-19-2015 (Note: joint clinical, statistics and virology review)
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	Filing: 4-16-2015 Primary: 6-29-2015
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested

Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	Filing:4-20-2015 Primary: 6-22-2015
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• Tertiary review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Secondary review (e.g., Branch Chief) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) (<i>indicate date for each review</i>)	Overall assessment/executive summary:6-30-2015 Primary Quality review: 6-29-2015 Facilities: 6-17-2015 Biopharm: 4-15-2015 Labeling: 6-29-2015
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	6-26-2015; page 35 of overall review
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> Facilities inspections (<i>action must be taken prior to the re-evaluation date</i>) (<i>only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i>)	<input checked="" type="checkbox"/> Acceptable Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) 	<input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>Notify CDER OND IO</i>)
<ul style="list-style-type: none"> • Finalize 505(b)(2) assessment 	<input type="checkbox"/> Done
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"> • Notify the CDER BT Program Manager 	<input checked="" type="checkbox"/> Done (<i>Send email to CDER OND IO</i>)
❖ For products that need to be added to the flush list (generally opioids): Flush List <ul style="list-style-type: none"> • Notify the Division of Online Communications, Office of Communications 	<input type="checkbox"/> Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input checked="" type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input checked="" type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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/s/

ELIZABETH G THOMPSON
07/27/2015

Thompson, Elizabeth

From: Thompson, Elizabeth
Sent: Wednesday, July 22, 2015 9:52 AM
To: Spears, Glen (glen.spears@abbvie.com)
Cc: Thompson, Elizabeth
Subject: NDA 207931: Information Request regarding carton/container labeling

Importance: High

Glen-

In our initial review of your container label and carton labeling we requested the following be done, "The lot number and expiration date are required on the immediate container per 21 CFR 201.10(i). Add both to the back of the packaging." The container label sent to us on 7/2 does not show either the lot or expiration date. Please verify that this information will be added to the container label per regulation prior to marketing.

Please provide a response before COB today.

Regards,

Beth

Chief, Project Management Staff
FDA/CDER/OAP/DAVP
301-796-0824

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/s/

ELIZABETH G THOMPSON
07/22/2015

From: Thompson, Elizabeth
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Subject: Technivie PREA PMR for agreement
Date: Tuesday, July 21, 2015 10:15:00 AM

Glen-

We removed (b) (4) from the PREA PMR. Here is the wording now. Please let me know if AbbVie agrees.

2934-1 Evaluate the safety and treatment response (using sustained virologic response as the primary endpoint) of TECHNIVIE (ombitasvir, paritaprevir, and ritonavir) in a cohort of pediatric subjects 3 to less than 18 years of age with chronic genotype 4 hepatitis C virus infection.

Final Protocol Submission: 07/31/2015 (submitted)

Study Completion: 04/30/2019

Final Report Submission: 08/31/2019

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
07/21/2015

From: [Thompson, Elizabeth](#)
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Cc: [Thompson, Elizabeth](#)
Subject: NDA 207931: DAVP label comments
Date: Tuesday, July 21, 2015 3:24:22 PM
Attachments: [DAVP proposed 7-21-2015.docx](#)
Importance: High

Glen-

Attached please find our comments on your last proposed version of the label. We agree with the changes proposed in the PI and have a couple of revisions proposed for the MG. Please let me know if you have any questions.

Regards,

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
07/21/2015

From: [Thompson, Elizabeth](#)
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Cc: [Thompson, Elizabeth](#)
Subject: NDA 207931: Final PMR/PMCs
Date: Tuesday, July 14, 2015 11:02:42 AM
Importance: High

Glen-

DAVP wants to provide the final draft PMR/PMCs for NDA 207931. We incorporated the dates you provided for the clinical virology PMR/PMC. There will only be a final study report submission date for those, as studies are ongoing.

Regarding the PREA PMR, we based the study off the PMR for Viekira Pak and used the same dates.

Please provide an official response with your agreement to these dates, or propose additional dates.

PMR XXXX-1 Evaluate the (b) (4) safety and treatment response (using sustained virologic response as the primary endpoint) of ombitasvir, paritaprevir, and ritonavir (TECHNIVIE) in a cohort of pediatric subjects 3 to less than 18 years of age with chronic genotype 4 hepatitis C virus infection.

Final Protocol Submission: 07/31/2015
Study/Trial Completion: 04/30/2019
Final Report Submission: 08/31/2019

PMR XXXX-2 Submit a final report on the persistence of treatment-emergent, ombitasvir or paritaprevir resistance-associated substitutions through Post-Treatment Week 48 in ongoing trials of HCV genotype 4 infected subjects.

Final Report Submission: 01/31/2018

PMC XXXX-3 Conduct a cell culture study to characterize the antiviral activity of ombitasvir against representative HCV subtype 4b isolates, including those with amino acid variability (relative to subtypes 4a and 4d) at NS5A positions 30 and 93.

Final Report Submission: 03/31/2016

Please let me know if you agree and I will send off so I can get them to submit agreement to NDA.

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
07/14/2015

From: [Thompson, Elizabeth](#)
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Cc: [Thompson, Elizabeth](#)
Subject: NDA 207931: DAVP proposed labeling
Date: Tuesday, July 14, 2015 10:14:43 AM
Attachments: [Technivie DAVP 7-14-15 proposed.docx](#)
Importance: High

Glen-

Attached please find DAVP comments/recommendations regarding Technivie labeling. Please let me know if you have any questions.

Please provide a response by Friday, July 17, 2015.

Regards,

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
07/14/2015

From: Thompson, Elizabeth
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Subject: RE: NDA 207931: request for mock up packaging
Date: Friday, July 10, 2015 8:05:00 AM

Glen-

Since different reviewers need to see this, please submit 3 copies of packaging.

Beth

From: Thompson, Elizabeth
Sent: Friday, July 10, 2015 7:59 AM
To: Spears, Glen (glen.spears@abbvie.com)
Cc: Thompson, Elizabeth
Subject: NDA 207931: request for mock up packaging
Importance: High

Glen-

I have followed up with our OPQ and OSE review team and they would still like to request a mock up of the Technivie packaging. Please provide this at your earliest convenience.

Regards,

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
07/10/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: July 1, 2015
NDA: 207931
PRODUCT: ombitasvir, paritaprevir, and ritonavir tablets
TO: Glen W. Spears, PhD, Director, Regulatory Affairs
FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP
SPONSOR: AbbVie Inc.
SUBJECT: NDA 207931 – Labeling Comments

Please refer to your New Drug Application (NDA) dated February 25, 2015 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ombitasvir, paritaprevir, and ritonavir tablets and to your submission of June 19, 2015 containing revised labeling in response to the Division's June 4, 2015 comments.

The Division's comments regarding the revised prescribing information are appended.

Please submit a response to NDA 207931 by COB on Tuesday, July 7, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
07/01/2015

**PeRC Meeting Minutes
June 10, 2015**

PeRC Members Attending:

Wiley Chambers
George Greeley
Freedra Crooner
Kristiana Brugger
Tom Smith
Daiva Shetty
Peter Starke
Lily Mulugeta
Robert "Skip" Nelson
Kevin Krudys
Shrikant Pagay
Rosemary Addy
Greg Reaman
Linda Lewis

Agenda

Non Responsive

9:20	NDA	207931	Technique (ombitasvir/paritaprevir/ritonavir) (Partial Waiver/Deferral) w/Agreed iPSP	Treatment of Infection	(b) (4) Chronic Hepatitis C Virus
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Non Responsive

Non Responsive

Technivie (ombitasvir/paritaprevir/ritonavir) Partial Waiver/Deferral/Plan

- Proposed Indication: Treatment of Genotype 4 Chronic Hepatitis C Virus Infection
- The Division noted that the plan is the same as the one agreed upon in the Agreed iPSP for Viekira Pak (approved for genotype 1 chronic HCV). This product should have the same PREA requirements as Viekira Pak without the dasabuvir component.
- The PeRC agreed with the plan as established in the Agreed iPSP.
- *PeRC Recommendations:*
 - The PeRC agreed with the Division to grant a waiver in pediatric patients less than 3 years of age because studies would be impossible or highly impractical and to the deferral in patients 3 to 17 years of age because the product is ready for approval in adults.

Non Responsive

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/s/

GETTIE AUDAIN
06/23/2015



NDA 207931

LABELING PMR/PMC DISCUSSION COMMENTS

AbbVie Inc.
Attention: Glen W. Spears, Ph.D.
Director, Regulatory Affairs
1 N. Waukegan Road, Dept. PA77/Bldg. AP30
North Chicago, IL 60064

Dear Dr. Spears:

Please refer to your New Drug Application (NDA) dated February 25, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ombitasvir, paritaprevir, and ritonavir tablets.

We also refer to our April 17, 2015 letter in which we notified you of our target date of August 4, 2015 for communicating labeling changes and/or postmarketing requirements/commitments in accordance with the "PDUFA Reauthorization Performance Goals and Procedures - Fiscal Years 2013 Through 2017".

We received your February 25, 2015 proposed labeling submission to this application, and have proposed revisions that are included as an enclosure. We request that you resubmit labeling that addresses these issues by June 19, 2015. The resubmitted labeling will be used for further labeling discussions.

Your proposed prescribing information (PI) must conform to the content and format regulations found at [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). Prior to resubmitting your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

For comments regarding the PI, please see the attached annotated label. In addition, we have the following comments regarding your carton/container labeling:

Container Label (Daily dose wallet pack)

1. The lot number and expiration date are required on the immediate container per 21 CFR 201.18 and 21 CFR 201.17, respectively. Add both to the back of the packaging.

Container Label and Carton Labeling (Daily, Weekly, and Monthly dose packs)

2. Consider removing the red color block from the strength statement and using no color, as the colored background may reduce the readability of the strength.

We have the following proposed Postmarketing Requirements/Commitments:

1. PMR: Conduct a study to characterize the persistence of viral populations with paritaprevir or ombitasvir resistance-associated substitutions in HCV GT4 infected subjects who experienced virologic failure with ombitasvir/paritaprevir/ritonavir with or without ribavirin. Note that data to address this PMR can come from M13-393 as well as other ongoing studies of HCV GT4 infected subjects.
2. PMC: Conduct a study to characterize the cell culture antiviral activity of ombitasvir against representative HCV subtype 4b isolates, including those with amino acid variability (relative to subtypes 4a and 4d) at NS5A positions 30 and 93.

If you have any questions, call me at (301) 796-0824.

Sincerely,

{See appended electronic signature page}

Elizabeth Thompson, M.S.
CDR, U.S. Public Health Service
Chief, Project Management Staff
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: Annotated label

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/s/

ELIZABETH G THOMPSON
06/04/2015

From: [Thompson, Elizabeth](#)
To: [Spears, Glen \(glen.spears@abbvie.com\)](mailto:glen.spears@abbvie.com)
Cc: [Thompson, Elizabeth](#)
Subject: NDA 207931: nonclinical request for information
Date: Wednesday, June 03, 2015 9:52:36 AM
Importance: High

Glen-

The nonclinical review team has the following comment:

Please provide the clinical and nonclinical paritaprevir exposure values (AUC) for the 2-DAA [and for comparison the original 3-DAA exposures (AUC)] used to calculate the exposure margins included in Sections 8 and 13 of the proposed label.

Please let me know if you have any questions regarding this request.

Regards,

Beth

Chief, Project Management Staff

FDA/CDER/OAP/DAVP

301-796-0824

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/s/

ELIZABETH G THOMPSON
06/03/2015



NDA 207931

**FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED**

AbbVie Inc.
Attention: Glen W. Spears, Ph.D.
Director, Regulatory Affairs
1 N. Waukegan Road, Dept. PA77/Bldg. AP30
North Chicago, IL 60064

Dear Dr. Spears:

Please refer to your New Drug Application (NDA) dated February 25, 2015, received February 25, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for ombitasvir, paritaprevir, and ritonavir tablets, 12.5 mg/75 mg/50 mg.

We also refer to your amendments dated March 4, 2015, March 13, 2015, April 3, 2015, April 10, 2015, April 13, 2015 and April 14, 2015.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Priority**. Therefore, the user fee goal date is August 25, 2015.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by August 4, 2015.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

In addition, we have the following comment for your consideration:

1. In the most recent communication (Mar 27, 2015), AbbVie indicated that an Access presentation is no longer planned for NDA 207931. If in the future an Access version is desired, it should be submitted as a supplement after action on the original NDA.

PRESCRIBING INFORMATION

Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances and
- FDA’s established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI) and Medication Guide. Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

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

Do not submit launch materials until you have received our proposed revisions to the package insert (PI) and Medication Guide, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

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.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult the Division of Antiviral Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a partial waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

We acknowledge receipt of your request for a partial deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial deferral request is denied.

If you have any questions, call Katherine Schumann, M.S., Senior Regulatory Project Manager, at (301) 796-1182.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

JEFFREY S MURRAY
04/17/2015

From: Schumann, Katherine
To: ["Spears, Glen"](#)
Cc: [Zumbrunnen, Troy L](#)
Subject: NDA 207931 - Clinical and Clinical Virology Information Requests
Date: Tuesday, April 14, 2015 2:54:00 PM

Dear Glen,

Please refer to your NDA 207931 submitted on February 25, 2015 for Technivie (ombitasvir, paritaprevir, and ritonavir) tablets. Please find below two requests for information from the review team:

Clinical

-

Please identify where in the study report these subjects are described or submit a brief narrative on each:

Bilirubin-related TEAEs of interest were identified in 3 subjects (2 noncirrhotic treated with 2-DAA + RBV; 1 cirrhotic treated with 2-DAA) and were all considered at least possibly related to DAA for all 3 subjects, and at least possibly related to RBV for the 2 noncirrhotic subjects.

Clinical Virology

-

HCV genotype 4 subtypes were identified based on phylogenetic analysis. According to the M13-393 clinical study report, these analyses included NS3, NS5A and NS5B. According to the resistance datasets, subtype was based on NS3 or NS5A sequences. Please clarify if there were any discordant subtyping results according to different genome targets evaluated, and if so, which results were considered for subgroup efficacy analyses and resistance datasets. If this detailed information is already included in the NDA, please indicate the study report or eCTD location.

Please respond via email to confirm receipt and let me know if you have any questions.

Warm Regards,
Katie

Katherine Schumann, M.S.
Senior Regulatory Project Manager
FDA/OMPT/CDER/OND/OAP
Division of Antiviral Products
10903 New Hampshire Ave., Bldg. 22, Room 6360
Silver Spring, MD 20993-0002
Phone: (301) 796-1182
Fax: (301) 796-9883
Email: Katherine.Schumann@fda.hhs.gov

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/s/

KATHERINE SCHUMANN
04/15/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: April 8, 2015
NDA: 207931
PRODUCT: ombitasvir, paritaprevir, and ritonavir tablets
TO: Glen W. Spears, PhD, Director, Regulatory Affairs
FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP
SPONSOR: AbbVie Inc.
SUBJECT: NDA 207931 – Biostatistics Information Request

Please refer to your New Drug Application (NDA) dated February 25, 2015 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ombitasvir, paritaprevir, and ritonavir tablets.

The review team has the following request for information:

The currently submitted dataset for HCV RNA viral load is derived (i.e., ETD.XPT). Please provide the raw HCV RNA data and the corresponding SAS program to convert the raw HCV RNA data to the derived data.

Please submit the requested information to the NDA by April 20, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
04/08/2015

From: Schumann, Katherine
To: ["Spears, Glen"](#)
Cc: [Gandhi, Virajkumar B](#)
Subject: Request for NDA 207931 site/investigator information by GT
Date: Monday, April 06, 2015 10:03:00 AM
Attachments: [image001.png](#)

Dear Glen,

I just left you a voice mail with the information below, but thought I would also send the request via email.

The review team would like AbbVie to provide the site/investigator information for M13-393 broken out by genotype for each site (# of GT4 subjects and # of GT1b subjects listed separately). The team is requesting this information as soon as possible. If you could email an excel file by COB today that would be greatly appreciated. If today is not possible, then we'd like the information as soon as it is available.

Please don't hesitate to email or call if you have any questions.

Warm Regards,

Katie

From: Spears, Glen [mailto:glen.spears@abbvie.com]
Sent: Tuesday, February 10, 2015 11:23 AM
To: Schumann, Katherine
Cc: Gandhi, Virajkumar B
Subject: NDA 207931 site/investigator information

Hi Katie!

In support of NDA 207931, the attached excel file contains a listing of all investigators for Study M13-393. The excel file contains contact information for each investigator as well as the number of subjects enrolled and discontinued for each investigator.

The NDA 207931 submission later this month will include a pdf version of the excel file in Module 1.11.3.

Best regards,

Glen

Glen W. Spears, Ph.D.
Director, Regulatory Affairs
Area and Affiliate Strategy, US/Canada

The AbbVie logo is displayed in a blue, lowercase, sans-serif font.

AbbVie Inc.
Bldg. AP-30
1 North Waukegan Road
North Chicago, IL 60064
OFFICE 847-938-7757
FAX 847-937-5852
CELL (b) (6)
EMAIL glen.spears@abbvie.com
abbvie.com

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/s/

KATHERINE SCHUMANN
04/06/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: April 1, 2015
NDA: 207931
PRODUCT: ombitasvir, paritaprevir, and ritonavir tablets
TO: Glen W. Spears, PhD, Director, Regulatory Affairs
FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP
SPONSOR: AbbVie Inc.
SUBJECT: NDA 207931 – Clinical Pharmacology Information Request

Please refer to your New Drug Application (NDA) dated February 25, 2015 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ombitasvir, paritaprevir, and ritonavir tablets.

The clinical pharmacology team has the following request for information:

For each DAA, please summarize the “new” in vitro information and “updated” in vitro information. For the purposes of this information request, “new” in vitro information refers to in vitro data that was not previously provided in NDA 206619 for VIEKIRA PAK (for example, in vitro studies conducted to assess the uptake of DAAs by the OCT1 transporter) and “updated” information refers to additional in vitro work conducted to supplement information provided in NDA 206619 for VIEKIRA PAK (for example assessment of OCT2 inhibition using pyrimethamine as an inhibitor is “updated” information because assessment of OCT2 inhibition using quinidine as an inhibitor was provided in NDA206619 for VIEKIRA PAK).

Please submit a response to NDA 207931 by April 17, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
04/01/2015



IND 120467
NDA 207931

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

AbbVie, Inc.
1 N. Waukegan Road
Dept. PA77/Bldg. AP30
North Chicago, IL 60064

ATTENTION: Glen W. Spears, Ph.D.
Director, Regulatory Affairs

Dear Dr. Spears:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act, and your New Drug Application (NDA) dated and received February 25, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ombitasvir, Paritaprevir, Ritonavir Tablets, 12.5 mg/75 mg/50 mg.

We also refer to:

- Your correspondence to your IND, dated and received January 15, 2015, requesting review of your proposed proprietary name, Technivie
- Your correspondence to your NDA, dated and received March 4, 2015, requesting review of your proposed proprietary name, Technivie

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

If **any** of the proposed product characteristics as stated in your above submissions are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Danyal Chaudhry, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3813. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager Katherine Schumann, at (301) 796-1182.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

AZEEM D CHAUDHRY
03/26/2015

TODD D BRIDGES
03/26/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: March 26, 2015
NDA: 207931
PRODUCT: ombitasvir, paritaprevir, and ritonavir tablets
TO: Glen W. Spears, PhD, Director, Regulatory Affairs
FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP
SPONSOR: AbbVie Inc.
SUBJECT: NDA 207931 – Response Regarding Proposed Packaging Change and Information Request

Please refer to your New Drug Application (NDA) dated February 25, 2015 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ombitasvir, paritaprevir, and ritonavir (OPR) tablets.

Proposed Packaging Change

Please refer to our information request of March 16, 2015 and your emails dated March 16, 2015 and March 20, 2015 containing additional information regarding your proposal to submit an amendment to NDA 207931 to change the packaging for the OPR tablets from a (b) (4) to a blister pack configuration.

The review team does not anticipate that submission of the blister packaging as proposed will substantially affect our review timelines; however, acceptability of the packaging to OPQ and DMEPA will be a review issue.

(b) (4)

NDA 206619 S-004

Please clarify whether any amendments are planned to the CBE-0 supplement submitted on February 12, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
03/26/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: March 16, 2015

NDA: 207931

PRODUCT: ombitasvir, paritaprevir, and ritonavir tablets

TO: Glen W. Spears, PhD, Director, Regulatory Affairs

FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP

SPONSOR: AbbVie Inc.

SUBJECT: NDA 207931 – Information Request Regarding Proposed Packaging Change

Please refer to your New Drug Application (NDA) dated February 25, 2015 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ombitasvir, paritaprevir, and ritonavir (OPR) tablets. Also refer to your email dated March 11, 2015 containing a proposal to submit an amendment to NDA 207931 to change the proposed packaging from [REDACTED] (b) (4) to a blister pack configuration.

We understand your proposal to be:

1. Revised plans for packaging of ombitasvir, paritaprevir and ritonavir (OPR) tablets such that the US product would be in blistercards constructed from the same materials as the OPR plus dasabuvir (D) packaging approved under NDA 206619.

[REDACTED] (b) (4)

To help us evaluate this proposal, please provide the following information by email.

1. A summary of the scientific reasons that leads AbbVie to conclude that the OPR blister package will provide equivalent or better protection relative to the OPR+D blister copackage. In the absence of stability data at this time on the OPR blister package, what other information supports this conclusion?
2. A timeline for submission of supportive stability data (early timepoints) on OPR tablets in the newly-proposed commercial packaging and/or other data to verify equivalent protection. Please also clarify when you anticipate launch supplies of the

OPR blister packs would be manufactured.

Please provide a response as soon as possible, no later than Thursday, March 19, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
03/16/2015

RECORD OF ELECTRONIC MAIL CORRESPONDENCE



Department of Health and Human Services
Public Health Service
Division of Antiviral Products

DATE: March 5, 2015

PRODUCT: Viekira Pak (ombitasvir, paritaprevir, ritonavir tablets; dasabuvir tablets) co-packaged for oral use

TO: Troy ZumBrunnen, PharmD, Director, Regulatory Affairs

FROM: Katherine Schumann, MS, Regulatory Project Manager, DAVP

SPONSOR: AbbVie Inc.

SUBJECT: Information Request - NDA 206619, NDA 207931, IND 103526, IND 101636, IND 108434, IND 120467, IND 122839

Please refer to your New Drug Application (NDA) dated April 21, 2014 for Viekira Pak and your NDA dated February 25, 2015 for ombitasvir, paritaprevir, and ritonavir tablets. Please also refer to your Investigational New Drug Applications (INDs) for dasabuvir, ombitasvir, and paritaprevir (alone and in combination).

Through our FAERS case reports, we have recently received reports of cardiac arrhythmias associated with use of some direct acting antiviral drugs, particularly in combination with amiodarone and/or beta blockers. Please review your global safety database for Viekira Pak and its component DAAs to identify cases of arrhythmia or symptoms consistent with arrhythmia (e.g., syncope, MI, etc) and submit your summary as soon as possible but no later than March 13, 2015.

Please respond via email to confirm receipt. We are providing the above information via electronic mail for your convenience. Please contact me at (301) 796-1182 or Katherine.Schumann@fda.hhs.gov if you have any questions regarding the contents of this transmission.

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
03/05/2015



NDA 207931

NDA ACKNOWLEDGMENT

AbbVie Inc.
Attention: Glen W. Spears, Ph.D.
Director, Regulatory Affairs
1 N. Waukegan Road, Dept. PA77/Bldg. AP30
North Chicago, IL 60064

Dear Dr. Spears:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: ombitasvir, paritaprevir, and ritonavir tablets

Date of Application: February 25, 2015

Date of Receipt: February 25, 2015

Our Reference Number: NDA 207931

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on April 26, 2015, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me at (301) 796-1182 or the Division's main number at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Katherine Schumann, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

KATHERINE SCHUMANN
03/04/2015



IND 120,467

MEETING MINUTES

AbbVie Inc.
Attention: Glen Spears, Ph.D.
Director, Regulatory Affairs
1 N. Waukegan Road
Dept. PA77/Bldg. AP30
North Chicago, IL 60064

Dear Dr. Spears:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for ombitasvir, paritaprevir, and ritonavir fixed-dose combination tablets.

We also refer to the teleconference between representatives of your firm and the FDA on October 9, 2014. The purpose of the meeting was to discuss the status of the ongoing clinical program, gain agreement on the content and format of NDA submission, gain agreement on the approach to PREA, and uncover any major unresolved potential issues.

A copy of the official minutes of the teleconference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Katherine Schumann, Regulatory Project Manager at (301) 796-1182.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA and Initial Comprehensive Multidisciplinary Breakthrough Therapy Meeting

Meeting Date and Time: October 9, 2014
Meeting Location: Teleconference

Application Number: IND 120,467
Product Name: ombitasvir, paritaprevir, and ritonavir tablets
Indication: Treatment of genotype 4 chronic hepatitis C virus infection
Sponsor/Applicant Name: AbbVie Inc.

Meeting Chair: Linda Lewis, MD
Meeting Recorder: Katherine Schumann, MS

FDA ATTENDEES

Office of Antimicrobial Products

John Farley, Deputy Director

Division of Antiviral Products

Debra Birnkrant, Division Director
Jeffrey Murray, Deputy Director
William Tauber, Acting Deputy Director of Safety
Linda Lewis, Medical Team Leader/Cross-Discipline Team Leader
Russell Fleischer, Medical Reviewer
Jules O'Rear, Clinical Virology Team Leader
Patrick Harrington, Clinical Virology Reviewer
Elizabeth Thompson, Chief, Project Management Staff
Katherine Schumann, Regulatory Project Manager

Office of Biostatistics

Lisa Rodriguez, Acting Biostatistics Team Leader
Karen Qi, Biostatistician

Office of Clinical Pharmacology

Islam Younis, Clinical Pharmacology Team Leader
Vikram Arya, Clinical Pharmacology Reviewer
Jeffry Florian, Pharmacometrics Team Leader

Office of New Drug Quality Assessment

Stephen Miller, CMC Team Lead

Office of Surveillance and Epidemiology

Felicia Duffy, DRISK

Office of Scientific Investigations

Antoine El Hage

SPONSOR ATTENDEES

Barry M. Bernstein, MD, Vice President, Infectious Disease Development
Rebecca Redman, MD, FIDSA, 2-DAA Project Director, HCV
Thomas J. Podsadecki, MD, 3-DAA Project Director, Antiviral Clinical Project Team
Niloufar Mobashery, MD, Senior Medical Director, Infectious Disease Development
Roula Qaqish, PharmD, Scientific Director, Infectious Disease Development
Meenal Patwardhan, MD, MHSA, Senior Medical Director and Product Safety Team Lead, Global Pharmacovigilance and Patient Safety
Mondira Bhattacharya, MD, Infectious Diseases Therapeutic Area Head, Pharmacovigilance and Patient Safety
Julie Kmiec, RN, BSN, Sr. Clinical Safety Manager, Safety Management, Antiviral/Anti-infective Development Teams
Christine Collins, PhD, Director, HCV Clinical Virology
Tami Pilot-Matias, PhD, Senior Principal Research Scientist, HCV Clinical Virology
Preethi Krishnan, PhD, Senior Research Scientist, HCV Clinical Virology
Jeff Arnold, Senior Study Project Manager, Clinical Program Development
Rajeev M. Menon, PhD, Director, Clinical Pharmacology and Pharmacometrics
Jennifer King, PharmD, Assistant Director, Clinical Pharmacology and Pharmacometrics
Carolyn M. Setze, Assistant Director, Statistics
Coleen Hall, Senior Research Statistician
Ivonne Falcon, MS, Principal Data Scientist, Data Sciences
Bruce Trela, PhD, Director, Preclinical Safety
Sou-Jen Chang, PhD, RAC, Associate Director, CMC Regulatory Affairs
Andrew Sansone, MS, Senior Director, Regulatory Affairs, US and Canada
Viraj Gandhi, MS, MBA, Senior Manager, Regulatory Affairs, US and Canada

1.0 BACKGROUND

AbbVie Inc. is developing a direct-acting antiviral (DAA) regimen for the treatment of genotype 4 (GT4) chronic hepatitis C virus (HCV) infection. The 2-DAA regimen includes the following drugs:

- paritaprevir (ABT-450), an NS3/4A protease inhibitor
- ombitasvir (ABT-267), an NS5A inhibitor

Ombitasvir and paritaprevir are coformulated with ritonavir, a CYP3A inhibitor used to increase concentrations of paritaprevir. The sponsor proposes this regimen in combination with RBV for

the indication of treatment of chronic HCV GT4 infection in adults who are either treatment-naïve or previously treated with pegIFN and RBV.

Ombitasvir and paritaprevir, in combination with a third DAA (dasabuvir, ABT-333), are currently being reviewed by the Agency under NDA 206619 for the treatment of genotype 1 HCV infection. The sponsor does not intend to [REDACTED] (b) (4)

The 2-DAA combination regimen was granted Breakthrough Therapy designation on June 30, 2014. Therefore, this meeting also serves as the Initial Comprehensive Multidisciplinary Breakthrough Therapy Meeting.

The dosage form proposed for the planned NDA is a fixed-dose combination, film-coated tablet of ombitasvir, paritaprevir, and ritonavir (the same as that used in the Phase 3 3-DAA program and submitted to NDA 206619). Because subjects in clinical trial M13-393 were administered the regimen as separate components, the sponsor plans to compare exposure data from the 2-DAA and 3-DAA clinical programs in the NDA.

This Type B, pre-NDA teleconference was requested on July 31, 2014 and the background package was received by DAVP on September 10, 2014. The purpose of the meeting is to discuss the efficacy and safety results from clinical trial M13-393 that will be submitted in the initial NDA to support the proposed indication, as well as the content and format of the planned NDA. The meeting should result in an agreement between the sponsor and the Division on the contents of a complete application.

On Wednesday, October 8, 2014, AbbVie informed the Division via email that they would like to focus discussion during the teleconference on the following questions:

- 2.6 Additional Comments, Clinical Pharmacology
- Question 6: Information on Treatment of GT4-Infected Adults with Compensated Cirrhosis
- CMC questions 1 and 2
- Question 11: 4-Month safety update

At the beginning of the teleconference, AbbVie also added Question 13, Proposed Package Insert to the agenda for discussion.

2.0 DISCUSSION

AbbVie's questions are presented below in ***bold italic*** font, DAVP's responses in standard font, and the meeting discussion in *italic* font.

2.1. Product Quality

Question 1: CMC Content and Cross-Reference to NDA 206619

The fixed-dose combination (FDC) coformulation of ombitasvir/paritaprevir/ritonavir (12.5 mg/75 mg/50 mg) in pink-colored, film-coated, oblong biconvex-shaped tablets debossed with "AV1" on one side to be used as the 2-DAA regimen for HCV GT4 infection (b) (4) FDC tablets in the 3-DAA regimen described in NDA 206619. Because the FDC tablets to be used for the 2-DAA regimen and the required stability data are (b) (4) those for the 3-DAA regimen, AbbVie proposes to cross-reference NDA 206619 in Module 1, Section 1.4.4 of the 2-DAA GT4 NDA for the entire Module 3 content and the Quality Overall Summary sections in Module 2 (Section 2.3.S and Section 2.3.P).

A new Introduction to Quality Overall Summary will be provided in Module 2 of the 2-DAA GT4 NDA. The Introduction to Quality Overall Summary will contain a list of the specific documents of the Quality Overall Summary that will be cross-referenced, along with the necessary Module 3 sections that will be included in the 2-DAA GT4 NDA to enable the cross referencing.

For the 2-DAA GT4 NDA, the proposed container/closure is a (b) (4) Draft carton and container labels for the (b) (4) will be provided in Module 1, Section 1.14.1.1 of the 2-DAA GT4 NDA (additional information concerning the proposed container/closure for the 2-DAA GT4 NDA can be found in Question 2).

In the June 12, 2014 NDA 206619 filing letter, FDA requested additional documents for cross-referencing ritonavir. AbbVie intends to include these corresponding documents for each drug substance (Module 3, Sections 3.2.S.1.1, 3.2.S.1.3, 3.2.S.2.1, 3.2.S.4.1 and 3.2.S.4.2 for ombitasvir, paritaprevir, and ritonavir) and the drug product (Module 2, Sections 3.2.P.1, 3.2.P.2.2, 3.2.P.3.1, 3.2.P.5.1 and 3.2.P.5.2) in the 2-DAA GT4 NDA. A one-page element indicating cross-referencing NDA 206619 and the above additional documents will be included at the beginning of each drug substance and drug product section of the 2-DAA GT4 NDA for ease of review.

Does the FDA agree with the proposed presentation and cross-referencing of the CMC content for the 2-DAA GT4 NDA submission?

FDA Response to Question 1:

We agree with the proposal to cross-reference NDA 206619 in Module 1 of the 2-DAA regimen, given that the ombitasvir/paritaprevir/ritonavir tablets (b) (4) to those covered by NDA 206619, in one of the packaging configurations described in that NDA. We also concur with your plans regarding the drug substance data that will be provided in the NDA for the 2-DAA treatment regimen (as outlined on pages 54-58 in the meeting package), as this information will facilitate our review of the application.

In addition to the information that will be submitted to 3.2.P.3.1 on the sites where the manufacturing, release and stability testing, packaging, and labeling of the tablets will be conducted, we understand your proposal will also include the Pharmaceutical Development, Drug Product Specification and Analytical Procedures sections. Given that some elements of

the control strategy for the tablets have evolved during the review of NDA 206619, it would be valuable to highlight those aspects in 3.2.P.2.2. If additional information is available at submission or during the review (e.g., methodology, methods validation, or results of (b) (4) testing within the tablet), we recommend that you note this in 3.2.P.2.2, and include representative data in Module 3 sections. If additional batches of the tablets have been manufactured beyond those included in NDA 206619, we recommend that representative information be included in section 3.2.P.5.4. We also recommend that you summarize the additional information discussed in this paragraph in the Quality Overall Summary of the 2-DAA NDA.

Question 1 Discussion:

AbbVie agreed that if additional tablet batches are available, the representative information will be provided in 3.2.P.5.4. AbbVie asked if it would be generally acceptable to submit new data to the 3-DAA NDA (NDA 206619) instead of the 2-DAA NDA (NDA 207931), and then provide cross-references in the appropriate Module 3 sections. This new information would also be noted in 3.2.P.2.2 in the 2-DAA NDA. DAVP responded that this proposal is acceptable.

AbbVie then proposed summarizing the additional information requested by DAVP under Question 1 as an introduction to the Quality Overall Summary (QOS) document instead of providing a comprehensive QOS in the 2-DAA NDA or a full update the 3-DAA QOS. DAVP responded that this proposal is acceptable.

DAVP also requested that AbbVie update the 3-DAA QOS to add a statement referring to the new information submitted to the 2-DAA NDA, so it will be clear in the future to someone reviewing the 3-DAA NDA that additional drug product information is available in the 2-DAA NDA.

AbbVie agreed to submit to IND 120,467 a specific written proposal regarding the contents of the "Introduction to the QOS" document to be submitted to the 2-DAA NDA, as well as the cross-referencing strategy. DAVP agreed to review and comment on this proposal, once submitted.

Question 2: Drug Product Packaging

The FDC coformulation of ombitasvir/paritaprevir/ritonavir (12.5 mg/75 mg/50 mg) in pink-colored, film-coated, oblong biconvex shaped tablets debossed with "AV1" on one side to be used as the 2-DAA regimen for HCV GT4 infection (b) (4). FDC tablets in the 3-DAA regimen described in NDA 206619; however, the proposed packaging is different. A (b) (4) is the proposed container/closure for the 2-DAA FDC ombitasvir/paritaprevir/ritonavir tablets whereas a copackaged blister pack inside a daily wallet pack has been proposed for the 3-DAA regimen (FDC ombitasvir/paritaprevir/ritonavir tablets and dasabuvir tablets). FDC drug product stability data in both the blister package (b) (4) have been included in the 3-DAA NDA 206619. AbbVie proposes to cross-reference NDA 206619 for the proposed

container/closure information and stability data. Draft carton and container labels (b) (4) will be provided in Module 1, Section 1.14.1.1 of the 2-DAA GT4 NDA.

Does the FDA have any comments on the proposed container/closure for the 2-DAA regimen?

FDA Response to Question 2:

We concur with your approach to cross-reference the container-closure information in NDA 206619 for information that would normally be included in Module 2 and in 3.2.P.7. Regarding the stability data that is provided in the NDA for the 2-DAA treatment regimen, it is possible that additional information may be available at submission or during the review. For example, additional measurements may have been conducted on stability samples based on revisions to the DP specification for the ombitasvir/paritaprevir/ritonavir tablets made during review of NDA 206619, or additional stability timepoints may have been reached. We recommend that you provide available data at the time of NDA submission, and indicate in the Quality Overall Summary whether any stability updates of this type might be possible during the review cycle.

Question 2 Discussion:

AbbVie agreed that if additional stability data is available beyond that submitted to NDA 206619 in response to the August 17, 2014 information request, it will be provided. AbbVie asked if this additional stability data can be submitted to NDA 206619, with a cross-reference provided to the 2-DAA NDA. DAVP responded that this acceptable, but that AbbVie should provide a summary of the new stability data in 3.2.P.2 and in the Introduction to the QOS, as discussed earlier.

DAVP commented that the review of NDA 206619 focused on the blister presentation, and that the data (b) (4) will be assessed during the review of the 2-DAA NDA. If possible, AbbVie should provide hyperlinks back to (b) (4) stability batches contained in NDA 206619. AbbVie responded that it would not be possible to provide hyperlinks, but they will provide a list of all stability batches and their location within NDA 206619. DAVP replied that this proposal is acceptable.

2.2. Pharmacology/Toxicology

Question 3: Nonclinical Information and Cross-Reference to NDA 206619

The proposed presentation and cross-referencing of the nonclinical information for the NDA submission are described in Sections 13.1 and 13.2.

Does the FDA agree with the proposed presentation and cross-referencing of the nonclinical information for the NDA submission?

FDA Response to Question 3:

Yes, DAVP agrees.

Question 3 Discussion:

No discussion occurred

2.3. Clinical

Question 4: Efficacy Data in HCV GT4-Infected Subjects from Clinical Study M13-393

During the January 29, 2014 3-DAA pre-NDA meeting and as described in the subsequent FDA meeting minutes issued on February 14, 2014, FDA agreed that the data from the single clinical Study M13-393 could be adequate to support an NDA submission for the 2-DAA regimen for HCV GT4. AbbVie proposes to utilize the data from Study M13-393, summarized in Section 13.3.3.2, to support an NDA submission for the 2-DAA regimen for the treatment of HCV GT4 infection.

Does the FDA agree that the efficacy data from the single clinical Study M13-393 could be sufficient to support the review and approval of the 2-DAA GT4 NDA?

FDA Response to Question 4:

Yes, DAVP agrees that efficacy data from the single clinical trial support submission of the 2-DAA GT4 NDA for possible approval, pending the formal review.

Question 4 Discussion:

No discussion occurred

Question 5: Rationale for the Use of the To-Be-Marketed Formulation

The rationale for the use of the to-be-marketed coformulated tablet is provided in Section 13.4.2. Does the FDA agree with proposed approach described?

FDA Response to Question 5:

Yes, DAVP agrees with the proposed approach.

Question 5 Discussion:

No discussion occurred

Question 6: Information on Treatment of GT4-Infected Adults with Compensated Cirrhosis

The efficacy and safety of the 2-DAA regimen have not been evaluated in HCV GT4-infected subjects with compensated cirrhosis. (b) (4)

Does the FDA agree with this approach?

FDA Response to Question 6:

No. (b) (4)

As previous comments indicate, we recommend that you amend the protocol for study M11-665 to add a 24-week arm of the 2-DAA + RBV regimen to ensure an optimal duration of treatment is identified for cirrhotic subjects with HCV GT4 infection.

Question 6 Discussion:

AbbVie acknowledged the DAVP comments provided regarding planned protocol M11-665 and agreed to add the requested 24-week arm, in addition to the planned 12- and 16-week arms. (b) (4)

DAVP responded that this proposal is not acceptable, and the regimens recommended in labeling will reflect the population studied in the trial submitted to the NDA (M13-393).

AbbVie acknowledged DAVP's response and proposed alternatively that interim data from M11-665 be submitted during review of the NDA to support use in subjects with compensated cirrhosis, should the 12- and/or 16- week arms demonstrate very high SVR rates. If the shorter duration arms result in very high SVR rates, DAVP agreed that AbbVie could request another discussion to determine whether submission of the data would be appropriate. DAVP added that the decision may depend upon how much time is left in the review cycle at the time when the data is available for submission.

2.4. Biostatistics

Question 7: Analysis-Ready Programs

AbbVie plans to provide the Analysis-Ready Programs (ARPs) listed in Appendix D for Study M13-393.

Does the FDA agree with the proposed list of ARPs to be provided?

FDA Response to Question 7:

Yes, DAVP agrees.

Question 7 Discussion:

No discussion occurred

2.5. Regulatory Questions

Question 8: Format and Content of the Integrated Summary of Efficacy (ISE) and Integrated Summary of Safety (ISS)

The proposed approach for the ISE and ISS in the 2-DAA GT4 NDA submission is described in Sections 13.5.1 and 13.5.2, respectively.

a) Does the FDA agree with the proposed format and content of the ISE?

b) Does the FDA agree with the proposed format and content of the ISS?

FDA Response to Question 8:

DAVP agrees with the proposed format and content of the ISE and ISS.

Question 8 Discussion:

No discussion occurred

Question 9: Format and Content for Module 2, Section 2.7.1 Biopharmaceutical Studies and Associated Analytical Methods

Does the FDA agree with the proposed data presentation and cross-referencing of the biopharmaceutical information for the 2-DAA GT4 NDA submission?

FDA Response to Question 9:

Yes, we agree.

Question 9 Discussion:

No discussion occurred

Question 10: Format and Content for Module 2, Section 2.7.2 Summary of Clinical Pharmacology Studies

One absolute bioavailability study (Study M14-229) for the coformulated tablet has been completed since the submission of NDA 206619 and will be described in Module 2, Section 2.7.2, Summary of Clinical Pharmacology Studies. There is no other new clinical pharmacology information for Module 2, Section 2.7.2 in the 2-DAA GT4 NDA. All relevant clinical pharmacology studies have been included in NDA 206619. AbbVie's proposal for describing the clinical pharmacology information for the 2-DAA GT4 NDA and AbbVie's proposal to provide a cross-reference in Module 1, Section 1.4.4 to the clinical pharmacology information in the 3-DAA NDA 206619 is described in Section 13.3.1.

Does the FDA agree with the proposed data presentation and cross-referencing of the clinical pharmacology information for the 2-DAA GT4 NDA submission?

FDA Response to Question 10:

Yes, DAVP agrees with the proposed approach.

Question 10 Discussion:

No discussion occurred

Question 11: 4-Month Safety Update

The 2-DAA GT4 NDA submission will include an interim clinical study report (CSR) for Study M13-393 based on a database lock that occurred on June 18, 2014. At the time of the database lock, all subjects had completed treatment and had reached at least post-treatment Week 12. Subjects are being followed from post-treatment Week 12 through study completion at post-treatment Week 48. HCV RNA, the emergence and persistence of resistant viral variants, and adverse events that are serious are being monitored during this period. A final CSR will be submitted when all subjects have reached post-treatment Week 48, and after the NDA review. Consistent with 3-DAA NDA 206619, for the 4-Month Safety Update, AbbVie proposes to provide summaries of all Study M13-393 post-treatment serious adverse events and post-treatment relapses that have occurred as of the NDA submission date. As described in Section 13.5.2, AbbVie intends to support the safety of the 2-DAA regimen with the safety data included in 3-DAA NDA 206619. AbbVie does not plan to update any of the 3-DAA NDA 206619 safety data as part of the 4-Month Safety Update.

Does the FDA agree with the proposed plan for the 4-Month Safety Update?

FDA Response to Question 11:

Yes, in general we agree with your proposal. Please clarify what data from the 3-DAA regimen will be used to support the 2-DAA regimen?

Question 11 Discussion:

AbbVie clarified that the 4-month safety update will only summarize new AEs and relapses from the 2-DAA program (M13-393) and will not include any new information from the 3-DAA trials. DAVP agreed with this proposed plan.

Question 12: Proposed Pharmacovigilance Plan

The proposed 2-DAA pharmacovigilance (PV) plan is provided in Appendix B and the justification is described in Section 13.3.5. The 2-DAA PV plan is the same as the 3-DAA PV plan that was included in Module 1, Section 1.16 of NDA 206619 except the 2-DAA PV plan addresses the HCV GT4-infected population rather than the HCV GT1-infected population. Considering the safety experience gained with the 3-DAA regimen in over 2000 subjects, and that the 3-DAA PV plan is driven by paritaprevir, which is common to both the 2-DAA and 3-DAA regimens, AbbVie believes the proposed approach for postmarketing safety monitoring for the 3-DAA regimen is also appropriate for the 2-DAA regimen.

Does the FDA have any comments on the proposed plan for postmarketing safety monitoring?

FDA Response to Question 12:

There are no comments on the proposed plan at this time. A final decision on the acceptability of the PV plan will be made following review of the safety data in the NDA. Please submit the proposed PV directed questionnaires in the NDA (Module 5).

Question 12 Discussion:

No discussion occurred

Question 13: Package Insert Content

The package insert for the 2-DAA GT4 NDA submission will be based on information in the 2-DAA GT4 NDA and the 3-DAA NDA 206619. (b) (4)



(b) (4)

(b) (4)

Does the FDA agree with this approach?

FDA Response to Question 13:

The package insert should be consistent with the information about the 2-DAA + RBV combination, and should represent a stand-alone document. (b) (4)

Question 13 Discussion:

AbbVie asked DAVP to comment on whether the proposed 2-DAA PI should reference the 3-DAA PI for annotation, where appropriate, (b) (4)

(b) (4) DAVP responded that referencing the 3-DAA PI is sufficient. AbbVie asked DAVP to further clarify (b) (4)

(b) (4) whether a general reference to the 3-DAA PI would suffice. DAVP agreed that a general reference to the 3-DAA PI would suffice.

Question 14: Overall Content of the eCTD NDA

The 2-DAA GT4 NDA submission will be provided in eCTD format as shown in Appendix A, in accordance with the FDA Guidance for Industry: Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications, Draft Guidance, July 2014, Revision 3.

a) Does the FDA agree that the proposed format and content for the 2-DAA GT4 NDA are adequate to be considered a complete application?

b) For the content of Module 1, Section 1.6.3 Correspondence Regarding Meetings, AbbVie proposes to cross-reference Module 1, Section 1.6.3 of NDA 206619 and include FDA correspondences starting from submission of the combination IND 120467 on April 08, 2014. Does the FDA agree with this proposal?

FDA Response to Question 14:

- a) In general, we agree. Please also see below for additional comments and requests.
- b) Yes, DAVP agrees.

Question 14 Discussion:

No discussion occurred

Question 15: Pediatric Research Equity Act (PREA) Requirement

An amendment to IND 120467 (eCTD Sequence/Serial 0011) to provide an initial pediatric study plan (iPSP) for the coformulated ombitasvir/paritaprevir/ritonavir tablets being developed for the treatment of HCV GT4 infection in adults was submitted on July 10, 2014. On August 12, 2014, the FDA provided comments on the iPSP. AbbVie agreed with these comments and the amended iPSP was submitted on September 03, 2014 to IND 120467 (eCTD Sequence/Serial 0027).

Does the FDA agree that [REDACTED] (b) (4) Does the FDA have any comments regarding the proposed pediatric plan?

FDA Response to Question 15:

Please refer to the FDA correspondence dated September 30, 2014 containing comments on your proposed iPSP submitted on July 10, 2014 and amended on September 3, 2014.

The iPSP does not itself meet the requirements of PREA but provides a plan for how studies required under PREA will be done. At the time of NDA submission, you are required to either submit pediatric studies or request a waiver or deferral. In the setting of an agreed upon iPSP, this request should mirror the plan previously submitted to the IND with any relevant updates, and should be included in the NDA submission.

Question 15 Discussion:

No discussion occurred

Question 16: Regulatory Information for Study M13-393

The data from the adequate and well-controlled Study M13-393 and the supportive information from the 3-DAA NDA 206619 are intended to provide substantial evidence of efficacy and safety to support approval of the NDA for the 2-DAA regimen plus RBV for HCV GT4 infection. Study M13-393 is considered a covered study and the supportive regulatory documentation (financial disclosure information and debarment certification) will be provided. Updating the regulatory documentation for the studies included in the 3-DAA NDA 206619 is not planned.

Does the FDA agree with the proposed plan to provide financial disclosure information and debarment certification information only for Study M13-393 in the 2-DAA GT4 NDA submission?

FDA Response to Question 16:

Yes, DAVP agrees.

Question 16 Discussion:

No discussion occurred

2.6 Additional Comments

Clinical Pharmacology:

1. Please include the following information in the NDA submission:
 - Evaluate exposure as a function of HCV genotype in POPPK analyses. Submit NONMEM control streams of the base and final model for population PK analysis. Model codes or control streams and output listings should be provided for all major model building steps, e.g., base structural model, covariates models, final model, and validation model. These files should be submitted as ASCII text files with *.txt extension (e.g.: myfile_ctl.txt, myfile_out.txt). Submit a model development decision tree and/or table which gives an overview of modeling steps.
 - Conduct exposure-response (E-R) analyses for safety using the pooled genotype 1 and genotype 4 populations and provide datasets and analysis codes used for these E-R analyses. Note whether there are difference is safety signals with respect to HCV genotype.
 - All analysis datasets used in non-model-based analysis should be submitted in the xpt format.

Discussion:

AbbVie suggested that for the second request (bullet #2), exposure-response analyses for safety would likely be of limited value due to the low number of events, as well as the fact that the formulation used for M13-393 provided lower exposures than the to-be-marketed formulation currently being reviewed under NDA 206619. AbbVie alternatively proposed to provide plots of safety events versus exposure. DAVP responded that the alternative proposal is reasonable, and that AbbVie should include in the NDA a rationale for their presentation of the information, as well as an interpretation of any safety signals in the context of the development program.

AbbVie acknowledged and agreed to the requests included in bullets #1 and #3.

Clinical Virology:

2. In the resistance datasets, please indicate subjects' HCV genotype 4 subtype in two separate columns based on the clinical screening assay (column: HCVGTSC) and phylogenetic analysis (column: HCVGTAN). Also, please include an additional column to report the country location of enrollment for each subject.

Discussion:

No discussion occurred.

3.0 PREA REQUIREMENTS

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 acknowledge your July 10, 2014 submission of an initial Pediatric Study Plan (iPSP) to IND 120,467, as amended on September 3, 2014. Your Agreed iPSP is expected to be submitted by January 6, 2015. Please plan to submit the Agreed iPSP to the NDA, along with the corresponding requests for waiver and/or deferral of pediatric studies.

4.0 PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. As you develop your proposed PI, we encourage you to review the labeling review resources on the *PLR Requirements for Prescribing Information* website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

5.0 MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided

in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

6.0 ISSUES REQUIRING FURTHER DISCUSSION

- Contents of Module 2 Quality Overall Summary and related cross-referencing to 3-DAA NDA
- Possible submission of M11-665 data in subjects with compensated cirrhosis, to be discussed when preliminary data (i.e. SVR12) are available from 12- and/or 16-week arms.

7.0 ACTION ITEMS

Action Item/Description	Owner	Due Date
Submit proposal for QOS and cross-referencing to IND 120,467	AbbVie Inc.	As soon as possible

8.0 ATTACHMENTS AND HANDOUTS

There were no attachments or handouts provided or referenced during the meeting.

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

/s/

JEFFREY S MURRAY
10/29/2014