# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 210455Orig1s000

# ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 113456

**MEETING PRELIMINARY COMMENTS**

Janssen Research & Development, LLC.
Attention: Karen Gerry, BSc
Associate Director, Global Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560

Dear Ms. Gerry:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) fixed dose combination tablet.

We also refer to your December 20, 2016, correspondence requesting a pre-NDA meeting to discuss and seek concurrence from the Agency regarding the proposed content and format of the NDA submission in support of the registration of the D/C/F/TAF FDC tablet for the treatment of HIV-1 infection.

Our preliminary responses to your meeting questions are enclosed.

You should provide, to the Regulatory Project Manager, a hardcopy or electronic version of any materials (i.e., slides or handouts) to be presented and/or discussed at the meeting.

In accordance with 21 CFR 10.65(e) and FDA policy, you may not electronically record the discussion at this meeting. The official record of this meeting will be the FDA-generated minutes.

If you have any questions, call me at (301) 796-0807.

Sincerely,

*{See appended electronic signature page}*

Myung-Joo Patricia Hong, M.S.
Senior Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Preliminary Meeting Comments

**FOOD AND DRUG ADMINISTRATION**
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# PRELIMINARY MEETING COMMENTS

**Meeting Type:** Type B
**Meeting Category:** pre-NDA

**Meeting Date and Time:** February 14, 2017, 1 - 2 PM
**Meeting Location:** Teleconference

**Application Number:** IND 113456
**Product Name:** darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) fixed dose combination tablet
**Indication:** Treatment of HIV-1 infection
**Sponsor/Applicant Name:** Janssen Research & Development, LLC.

**Introduction:**

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for February 14, 2017, 1 PM, between Janssen Research & Development, LLC. and the Division of Antiviral Products. We are sharing this material to promote a collaborative and successful discussion at the meeting. The meeting minutes will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments following substantive discussion at the meeting. If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda. Contact the Regulatory Project Manager (RPM) if there are any major changes to your development plan, the purpose of the meeting, or the questions based on our preliminary responses, as we may not be prepared to discuss or reach agreement on such changes at the meeting.

## 1.0 BACKGROUND

Due to an unmet medical need for a protease inhibitor (PI)-based single-tablet regimen, Janssen (Sponsor) and Gilead Sciences, Inc. (Gilead) have co-formulated the nucleotide reverse transcriptase inhibitor (NtRTI) tenofovir (TFV)-prodrug tenofovir alafenamide (TAF, 10 mg) with the PI darunavir (DRV, D; 800 mg), the pharmacokinetic (PK) enhancer cobicistat (COBI, C; 150 mg), and the nucleoside reverse transcriptase inhibitor (NRTI) emtricitabine (FTC, F; 200 mg) to form the first PI-based fixed-dose combination (FDC) single-tablet option for oral once daily use (D/C/F/TAF). The D/C/F/TAF tablet offers the additional advantage of including an N(t)RTI backbone that has an improved renal and bone safety profile compared with a tenofovir disoproxil fumarate (TDF)-containing backbone. The development program of the D/C/F/TAF FDC product is based on six clinical studies conducted with the FDC tablet in adults:

- Two pivotal Phase 3 studies (TMC114IFD3013 and TMC114FD2HTX3001), which are still ongoing;
    - Study TMC114FD2HTX3001 in HIV-infected, ART-naïve adult subjects
    - Study TMC114IFD3013 in HIV-infected, virologically-suppressed adult subjects
- One completed Phase 2 study conducted by Gilead; and
- Three completed Phase 1 studies, of which two were conducted by the Sponsor and one by Gilead.

This program is complemented, as appropriate, by studies from the development programs of the individual compounds, i.e., studies conducted in adolescents, studies to assess the QT effects, studies in special populations such as subjects with renal impairment, hepatic impairment and subjects co-infected with hepatitis B, and drug-drug interaction studies.

Gilead has transferred further development of the FDC tablet to Janssen and, subject to regulatory approval, the manufacturing, registration, distribution and commercialization of the product worldwide.

The primary purpose of the meeting is to discuss and seek concurrence from the Agency regarding the proposed content and format of the NDA submission in support of the registration of the D/C/F/TAF FDC tablet for the treatment of HIV-1 infection.

The proposed NDA submission is targeted for September 2017.

## 2.0 DISCUSSION

Your questions are in ***bold italics*** and DAVP comments are in standard font.

### 2.1. Pharmacology/Toxicology

***Q1: As there are no new non-clinical studies included in this NDA, the Sponsor will only provide a non-clinical overview in Module 2.4. Does the Division agree with this approach?***

**FDA Response:** Yes, we agree with your proposal.

### 2.2. Clinical Pharmacology

***Q2: The Sponsor plans to align the drug-drug interaction information and recommendations for the D/C/F/TAF FDC with the approved Prescribing Information for the respective separate agents. Additional drug-drug interactions based on an up-to-date status of new drug approvals and/or Prescribing Information updates for relevant concomitant drugs will be included, as applicable. Since D/C/F/TAF is a complete treatment regimen for HIV-infection, drug-drug interaction data with other HIV antiretrovirals (ARVs) will however not be included in the D/C/F/TAF FDC Prescribing Information. Does the Division agree with this approach?***

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