CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208984Orig1s000
022128Orig1s017

OTHER REVIEW(S)

Division of Antiviral Products

REGULATORY PROJECT MANAGER LABELING REVIEW

Application: NDA 208984 and NDA 22128/S-17

Name of Drug: SELZENTRY (maraviroc) oral solution 20 mg/ml
SELZENTRY (maraviroc) 25 mg and 75 mg tablets

Applicant: ViiV Healthcare Company

Labeling Reviewed

Submission Date: November 1, 2016

Receipt Date: November 1, 2016

Background and Summary Description:

Selzentry (maraviroc) is a CCR5 co-receptor antagonist approved in the US on August 6, 2007 for the treatment of only CCR5-tropic HIV-1 infection in adults. In response to their PREA PMR 1357-2 and their Written Request, Viiv submitted a NDA 208984 and an efficacy supplement to NDA 22128 to expand the patient population to include pediatric patients 2 years of age and older weighing at least 10 kg. A 20 mg/ml oral solution, 25 mg tablet, and 75 mg tablet are being provided for use in the pediatric population.

This RPM labeling review compares ViiV's most recent labeling dated November 1, 2016 to the last approved Selzentry® labeling dated April 21, 2015 (NDA 22128/S-15).

Review

GLOBAL CHANGES
New Tables were added, therefore Table numbers have changed. Cross references were updated to reflect new tables and subsection headings.

Under "HIGHLIGHTS OF PRESCRIBING INFORMATION" the following changes were proposed:

SELZENTRY® **(maraviroc) tablets, for oral use**
SELZENTRY® (maraviroc) oral solution

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/s/

ANDREW A GENTLES
11/04/2016

KAREN D WINESTOCK
11/04/2016

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	November 3, 2016
Requesting Office or Division:	Division of Antiviral Products (DAVP)
Application Type and Number:	NDA 22128/S-17 and NDA 208984
Product Name and Strength:	Selzentry (maraviroc), Oral Solution and Tablets 20 mg/mL and 25 mg, 75 mg
Submission Date:	October 27, 2016
Applicant/Sponsor Name:	Viiv Healthcare
OSE RCM #:	2016-1286-1 and 2016-1287-1
DMEPA Primary Reviewer:	Mónica Calderón, PharmD, BCPS
DMEPA Team Leader:	Vicky Borders-Hemphill, PharmD

1 PURPOSE OF MEMO

Viiv Healthcare has submitted the revised container label, carton labeling, and instructions for use (Appendix A) for Selzentry in response to recommendations we made during a previous label and labeling review.[1] Thus, the Division of Antiviral Products (DAVP) requested that we review the revised labels and labeling to determine if they are acceptable from a medication error perspective.

2 CONCLUSION

[1] Calderon M. Label and Labeling Review for Selzentry (NDA NDA 22128/S-17 and NDA 208984). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2016 August 10. 32 p. OSE RCM No.: 2016-1286 and 2016-1287.

The revised container labels, carton labeling, and instructions for use for Selzentry are acceptable from a medication error perspective.

Of note, we recommended the removal of all error prone symbols in the tables in the Dosage and Administration section of the Prescribing Information; however, the Sponsor proposed to retain them rather than using wording in the column headings of all tables for consistency and readability. They also stated, the FPI is for physician information vs. patient information and the symbols should be readily understood. We agreed with the Sponsor to keep the symbols in the table for readability but will monitor for post market confusion. We have no further recommendations at this time.

APPENDIX A. LABEL AND LABELING SUBMITTED ON OCTOBER 27, 2016

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/s/

MONICA M CALDERON
11/03/2016

BRENDA V BORDERS-HEMPHILL
11/03/2016

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Pediatric and Maternal Health
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring, MD 20993
Tel 301-796-2200
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Pregnancy and Lactation Labeling Rule (PLLR) Labeling Review

Date: 10-07-2016

From: Leyla Sahin, MD
Medical Officer, Maternal Health
Division of Pediatric and Maternal Health

Through: Tamara Johnson, M.D., M.S.
Team Leader, Maternal Health
Division of Pediatric and Maternal Health

Lynne P. Yao, MD
Director, Division of Pediatric and Maternal Health

To: Division of Antiviral Products

Drug: Selzentry (maraviroc) NDA 208984 and 22128/S-17

Approved indication: Combination antiretroviral treatment of adults infected with only CCR5-tropic human immunodeficiency virus (HIV-1)

Subject: Pregnancy and Lactation Labeling Rule (PLLR) Conversion as part of Efficacy Supplement

Applicant: ViiV Healthcare

Materials Reviewed:
- Applicant's Proposed Labeling and Summary of Clinical Safety (sections relevant to Pregnancy and Lactation); Current Selzentry labeling, approved 4-2015
- Antiretroviral Pregnancy Registry data (6-2016 Report)
- Department of Health and Human Services Panel 2016 Perinatal HIV Guidelines

Consult Questions: Please assist with pregnancy and lactation labeling

INTRODUCTION

The applicant submitted an efficacy supplement for Selzentry (maraviroc) on May 6, 2016, that proposes to expand the patient population to include pediatric subjects from 2 to less than 18 years of age for the treatment of CCR5-tropic human immunodeficiency virus (HIV-1) in combination with other antiretrovirals. The supplement also includes Pregnancy and Nursing Mothers labeling revisions in the format of the Pregnancy and Lactation Labeling Rule. The Division of Antiviral Products (DAVP) consulted the Division of Pediatric and Maternal Health (DPMH) on June 21, 2016 to review the applicant's proposed labeling revisions.

BACKGROUND

Product Background

Selzentry (maraviroc) was approved in 2007 and is a CC chemokine receptor type 5 (CCR5) co-receptor antagonist indicated for combination antiretroviral treatment of adults infected with only CCR5-tropic human immunodeficiency virus (HIV-1). Selzentry is a selective, slowly reversible, small molecule antagonist of the interaction between human CCR5 and HIV-1 gp120. Blocking this interaction prevents CCR5-tropic HIV-1 entry into cells.

Currently approved Selzentry's pregnancy labeling includes only nonclinical data that showed no adverse developmental outcomes in rats and rabbits at exposures 20 and 5 fold, respectively, the human dose of maraviroc, based on AUC.

Clinical Guidelines

Based on current national guidelines for treatment of HIV, safety and pharmacokinetic data on maraviroc use in pregnancy are insufficient to recommend use in antiretroviral (ARV)-naive pregnant women. National guidelines state that use of maraviroc can be considered for pregnant women who have failed therapy with several other classes of ARV drugs after consultation with HIV and obstetric specialists.[1]

Pregnancy and Lactation Labeling Rule (PLLR)

The Pregnancy and Lactation Labeling Rule (PLLR) went into effect on June 30, 2015.[2] The PLLR requirements include a change to the structure and content of labeling for human prescription drug and biologic products with regard to pregnancy and lactation. Additionally, information on pregnancy testing, contraception, and infertility that has been located in other sections of labeling are now presented in a new subsection, 8.3 Females and Males of Reproductive Potential, under Use in Specific Populations (8). Specifically, the pregnancy categories (A, B, C, D and X) will be removed from all prescription drug and biological product labeling and a new format will be required for all products that are subject to the 2006 Physicians

[1] Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1- Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States June 2016.

[2] Content and Format of Labeling for Human Prescription Drug and Biological Products, Requirements for Pregnancy and Lactation Labeling (79 FR 72063, December 4, 2014).

Labeling Rule, to include information about the risks and benefits of using these products during pregnancy and lactation.

REVIEW OF SUBMISSION

Pregnancy

Nonclinical Experience

No new nonclinical data were submitted with this supplement. The nonclinical section for Pregnancy was revised to conform to PLLR by DAVP Pharmacology/Toxicology reviewer, Dr. Christopher Ellis.

Applicant's Pregnancy Safety Review

1. Assessment of data from the June 2016 Antiretroviral Pregnancy Registry (APR) Interim Report[3]

As of December 31, 2015, the APR received 25 prospective reports of live births following exposure to maraviroc containing regimens in pregnancy that include 0 birth defects out of 20 live births exposed during the first trimester and 0 birth defects out of 5 live births exposed during the second/third trimester.

2. Literature Review

Safety data on maraviroc use in pregnancy are limited to two published case reports. One woman received maraviroc during the first trimester and through the end of pregnancy, and another woman received maraviroc and etravirine from week 29 of pregnancy, in addition to her existing treatment with tenofovir disoproxil fumurate/emtricitabine and darunavir/ritonavir. Both had normal infant outcomes.[4,5]

There is a published pharmacokinetic (PK) study of 18 pregnant women (includes 2 first trimester exposures) that showed that although overall maraviroc exposure was 28% – 30% lower during the third trimester of pregnancy, minimum concentration (C_{trough}) was reduced to a lesser extent and met the target average and minimum concentrations needed to provide virologic inhibition.[6]

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[3] http://www.apregistry.com

[4] Jeantils, V., Tigazin, A., Lachassine, E., Rodrigues, A., Bentata, M., & Peytavin, G. (2011). Favourable Outcome of a Pregnancy with a Maraviroc-Containing Regimen. Journal of AIDS & Clinical Research, 2 (6).

[5] Calcagno, A., Trentini, L., Marinaro, L., Montrucchio, C., D 'avolio, A., Ghisetti, V., Bonora, S. (2013). Transplacental passage of etravirine and maraviroc in a multidrug experienced HIV-infected woman failing on darunavir-based HAART in late pregnancy. J Antimicrob Chemother.

[6] Colbers A, Best B, Schalkwijk S, et al. Maraviroc Pharmacokinetics in HIV-1-Infected Pregnant Women. Clin Infect Dis. 2015 Nov 15;61 (10):1582-9.

Reviewer comment
The applicant did not propose the inclusion of any PK data in labeling and per DAVP's clinical pharmacology reviewers, the applicant did not provide raw data from the published PK paper; therefore, the applicant will need to submit the data for review after this review cycle.

DPMH performed a search of published literature on the safety of maraviroc in pregnancy and did not identify any additional publications.

3. Applicant's Safety Database

The applicant performed a cumulative review of their Global Safety Database through October 31, 2015 for cases of maraviroc use during pregnancy. Cumulatively, there are 80 cases of maraviroc exposure (includes 6 paternal exposures), based on data from the APR, case reports from the literature, and spontaneous reports. The following outcomes are reported:

- 36 live births
    - includes 2 birth defects
        - polydactyly (maraviroc exposure occurred starting at 36 weeks gestation)
        - unilateral multicystic kidney with vesico-ureteral reflux (maraviroc exposure occurred starting at 18 weeks gestation and abnormalities were detected on ultrasound prior to initiation of maraviroc)
- 8 elective terminations (no birth defects or unknown if birth defect present)
- 11 spontaneous abortions (no birth defects or unknown if birth defect present)
- 1 abortion, unspecified
- 2 ectopic pregnancies
- 22 ongoing pregnancies and/or lost to follow up or unknown

The applicant concludes that available data are insufficient to draw any conclusions on the safety of maraviroc use during pregnancy.

Reviewer comment
The two birth defect cases are not likely to be due to maraviroc exposure as exposure in both cases occurred outside the etiologically relevant period of organogenesis.

DPMH concurs with the applicant's conclusion that available data are insufficient to draw any conclusions on the safety of maraviroc use during pregnancy. The applicant should follow-up on ongoing pregnancies.

Lactation

Nonclinical Experience

No new nonclinical data were submitted with this supplement. The nonclinical section for Lactation was revised to conform to PLLR by DAVP Pharmacology/Toxicology reviewer, Dr. Christopher Ellis.

Applicant's Lactation Safety Review
There are no published data on the safety of maraviroc in lactation and no cases in the applicant's safety database.

Reviewer comment
DPMH performed a search of published literature on the safety of maraviroc in lactation and did not identify any publications.

DISCUSSION

Pregnancy
Available maraviroc data are limited and not sufficient to inform the risk associated with use during pregnancy. DPMH concurs with the applicant's proposal to include a risk statement in Selzentry labeling that reflects that available data are not sufficient to inform a drug-associated risk of birth defects or miscarriage.

Lactation
National guidelines from the Department of Health and Human Services[1] and the CDC[7] recommend that HIV infected women in the U.S. not breastfeed because of the risk of transmission of HIV to their infant and the availability of safe and sustainable infant feeding alternatives. Similar to labeling of other antiretroviral agents, it is appropriate to include language in Selzentry labeling that reflects national guidelines for HIV infected women to not breastfeed.

CONCLUSIONS

The Pregnancy and Lactation subsections of Selzentry labeling were structured to be consistent with the PLLR. DPMH has the following recommendations for Selzentry labeling:

- **8.1 Pregnancy**
  - The "Pregnancy" subsection of Selzentry labeling was formatted in the PLLR format to include "Pregnancy Registry", "Risk Summary", and "Data" headings.

- **8.2 Lactation**
  - The "Lactation" subsection of Selzentry labeling was formatted in the PLLR format to include the "Risk Summary" and "Data" sections.

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[7] Centers for Disease Control and Prevention, Health Resources and Services Administration, National Institutes of Health, American Academy of HIV Medicine, Association of Nurses in AIDS Care, International Association of Providers of AIDS Care, the National Minority AIDS Council, and Urban Coalition for HIV/AIDS Prevention Services. *Recommendations for HIV Prevention with Adults and Adolescents with HIV in the United States, 2014*. 2014. http://stacks.cdc.gov/view/cdc/26062. December 11, 2014.

DPMH LABELING RECOMMENDATIONS

See final labeling for all of the labeling revisions negotiated with the applicant.

HIGHLIGHTS OF PRESCRIBING INFORMATION
USE IN SPECIFIC POPULATIONS
Lactation: Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission. (8.2)

8.1 Pregnancy
Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to SELZENTRY during pregnancy (b) (4) are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) 1-800-258-4263.

Risk Summary

Limited data on the use of SELZENTRY during pregnancy from the APR and case reports are not sufficient to inform a drug-associated risk of birth defects and miscarriage. In animal reproduction studies, no evidence of adverse developmental outcomes was observed with maraviroc. (b) (4) during organogenesis (b) (4), systemic exposures (AUC) to maraviroc were approximately 20 times (rats) and 5 times (rabbits) the exposure in humans at the recommended 300 mg twice-daily dose. In the rat pre- and post-natal development study, maternal systemic exposure (AUC) to maraviroc was approximately 14 times the exposure in humans at the recommended 300 mg twice-daily dose *[see Data]*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data
Animal Data

Maraviroc was administered orally to pregnant rats (up to 1,000 mg per kg per day) and rabbits (up to 75 mg per kg per day) on gestation Days 6 to 17 and 7 to 19, respectively. No adverse effects on embryo-fetal development were observed at these dose levels, resulting in exposures (AUC) approximately 20 times (rats) and 5 times (rabbits) higher than human exposures at the recommended daily dose. In the rat pre- and post-natal development study, maraviroc was administered orally at up to 1,000 mg per kg per day on gestation Day 6 to lactation/post-partum Day 20, with development of the offspring (including fertility and reproductive performance) unaffected by maternal administration of maraviroc at an exposure (AUC) approximately 14 times higher than human exposure at the recommended daily dose.

8.2 Lactation

Risk Summary

The Centers for Disease Control and Prevention recommend that HIV-infected mothers not breastfeed their infants to avoid postnatal transmission of HIV.

There are no data on the presence of maraviroc in human milk, the effects on the breastfed infant, or the effects on milk production. When administered to lactating rats, maraviroc was present in milk *[see Data]*. Because of the potential for (1) HIV transmission (in HIV-negative infants), (2) developing viral resistance (in HIV-positive infants), and (3) serious adverse reactions in a breastfed infant similar to those seen in adults, instruct mothers not to breastfeed if they are receiving SELZENTRY.

Data

Maraviroc (and related metabolites) was excreted into the milk of lactating rats following a single oral dose of maraviroc (100 mg per kg) on lactation Day 12, with a maximal milk concentration achieved one hour post-administration at a milk concentration approximately 2.5 times that of maternal plasma concentrations. (b) (4)

(b) (4)

17 PATIENT COUNSELING INFORMATION

Pregnancy

Inform patients that there is insufficient data on the safety of SELZENTRY in pregnancy. Inform patients that there is an antiretroviral pregnancy registry that monitors pregnancy outcomes in women exposed to SELZENTRY during pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation

Instruct women with HIV-1 infection not to breastfeed because HIV-1 can be passed to the (b) (4) in breast milk *[see Use in Specific Populations (8.2)]*.

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/s/

LEYLA SAHIN
10/07/2016

TAMARA N JOHNSON
10/07/2016

LYNNE P YAO
10/11/2016

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	October 7, 2016
To:	Debra Birnkrant, MD Director **Division of Antiviral Products (DAVP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Morgan Walker, PharmD, MBA, CPH Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** L. Shenee' Toombs, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG) and Instructions for Use (IFU)
Drug Name (established name), Dosage Form and Route, Application Type/Number:	SELZENTRY (maraviroc) tablets, for oral use, NDA 022128/S-017 SELZENTRY (maraviroc) oral solution, NDA 208984
Applicant:	ViiV Healthcare

1 INTRODUCTION

On May 6, 2016, ViiV Healthcare submitted for the Agency's review a New Drug Application (NDA) 208984 for SELZENTRY (maraviroc) oral solution. This submission references SELZENTRY (maraviroc) tablets which are currently approved under NDA 022128. ViiV Healthcare also submitted for the Agency's review efficacy supplement NDA 022128/S-017 for SELZENTRY (maraviroc) tablets which seeks approval for two lower strengths of maraviroc tablets (25 mg and 75 mg). Both submissions support the expansion of the approved indication to include patients 2 years of age and older weighing at least 10 kg.

SELZENTRY (maraviroc) tablets were originally approved on August 6, 2007 and currently are indicated in combination with other antiretroviral agents, for adult patients infected with only CCR5-tropic HIV-1.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Antiviral Products (DAVP) on May 31, 2016, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) and Instructions for Use (IFU) for SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and DMEPA deferred to DMPP to provide IFU review comments.

2 MATERIAL REVIEWED

- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution MG received on May 6, 2016, and received by DMPP on September 21, 2016.
- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution MG received on May 6, 2016, and received by OPDP on September 28, 2016.
- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution IFU received on May 6, 2016, and received by DMPP on September 21, 2016.
- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution IFU received on May 6, 2016, and received by OPDP on September 28, 2016.
- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution Prescribing Information (PI) received on May 6, 2016, revised by the Review Division throughout the review cycle, and received by DMPP on September 21, 2016.
- Draft SELZENTRY (maraviroc) tablets and SELZENTRY (maraviroc) oral solution Prescribing Information (PI) received on May 6, 2016, revised by the

Review Division throughout the review cycle, and received by OPDP on September 28, 2016.

- Approved SELZENTRY (maraviroc) tablets labeling dated April 21, 2015.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the MG and IFU the target reading level is at or below an 8th grade level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We have reformatted the MG document using the Arial font, size 10.

In our collaborative review of the MG and IFU we have:

- simplified wording and clarified concepts where possible
- ensured that the MG and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG and IFU meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The MG and IFU are acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the MG and IFU is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the MG and IFU.

Please let us know if you have any questions.

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/s/

MORGAN A WALKER
10/07/2016

LATOYA S TOOMBS
10/07/2016

BARBARA A FULLER
10/07/2016

LASHAWN M GRIFFITHS
10/07/2016

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: October 7, 2016

To: Andrew Gentles, Regulatory Project Manager
Division of Antiviral Products (DAAAP)

From: L. Shenee Toombs, Regulatory Review Officer (OPDP)

CC: Olga Salis, Senior Regulatory Health Project Manager (OPDP)
Michael Wade, Regulatory Health Project Manager (OPDP)

Subject: NDA 208984
NDA 22128/S-017
OPDP labeling comments for SELZENTRY (maraviroc) tablets, for oral use, and oral solution
Labeling Review

OPDP has reviewed the proposed package insert (PI), Medication Guide, Instructions for Use (IFU), and carton and container labeling for SELZENTRY (maraviroc) tablets, for oral use, and oral solution (Selzentry) that was submitted for consult on June 1, 2016. Comments on the proposed PI are based on the version sent via email from Andrew Gentles (RPM) on September 28, 2016 entitled "208984draft-proposed.docx" and the draft carton/container labeling submitted September 2, 2016.

Comments regarding the PI are provided on the marked version below.

OPDP has no comments on the draft carton and container labeling at this time.

Please note that comments on the Medication Guide and Instructions for Use will be provided under separate cover as a collaborative review between OPDP and the Division of Medical Policy Program (DMPP).

Thank you for the opportunity to comment.

If you have any questions, please contact Shenee' Toombs at (301) 796-4174 or latoya.toombs@fda.hhs.gov.

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LATOYA S TOOMBS
10/07/2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES **M E M O R A N D U M**

Food and Drug
Administration
Office of Device
Evaluation White
Oak Building 66
10903 New Hampshire Ave.
Silver Spring, MD 20993

Intercenter Consult Memorandum

Device Constituent Part Design Review: CDER PAS NDA 022555 - CDRH ICC1600310

Date: October 5, 2016

To: Stephen Miller
Branch (PMBI)
Division of (DPMAI)
Office of (OLDP)
Office of Pharmaceutical Quality (OPQ)
Center for Drug Evaluation and Research (CDER)

From: Sarah Mollo
General Hospital Devices Branch (GHDB),
Division of Anesthesiology, General Hospital
Respiratory, Infection Control, & Dental Device
(DAGRID),
Office of Device Evaluation (ODE),
Center for Devices and Radiological Health (CDRH)

Subject: Device Constituent Part Design Review: CDER NDA 208984 - CDRH ICC1600393; CDER priority review of oral solution; CDRH review of device constituents oral syringe vial-adaptor

Recommendation: CDRH recommends approval based on review of the device constituent of the combination product

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I. Recommendation and Summary

The device consultant authoring this review memorandum has performed a design review of submission materials intended to support the safety and functionality of the device constituent parts of the subject combination product. This review did not cover manufacturing of the device constituent parts.

The review of submission documentation by CDRH/ODE found that the design requirements of the device components are acceptable and that essential performance of the final finished device can be assured with a reasonable degree of certainty. Essential performance elements of the device under review by the consultant were considered to be:

- Dose accuracy
- Compatibility of components
- Biocompatibility of non-primary closure components

Review of this information found that there are sufficient design control documentation and verification activities for the device constituent part of the combination product to recommend approval.

II. Submission Content Reviewed by CDRH/ODE

The CDRH/ODE reviewers performed an evaluation of the design of the device constituent parts of the Maraviroc solution combination product. This evaluation covered the intended design and design control information for the subject device constituent part.

This review covered the following review content:

- Inspection of sponsor's design input activities
- Inspection of sponsor's design verification activities
- Confirmation of standards conformance, where relied upon
- Inspection of test methods and results of bench top testing completed
- Risk analysis

This review covered the following review materials:

- 3.2.P.7 Container Closure System- Packaging component Description
- 3.2.P.7.2 Container Closure System- Specifications
- 3.2.P.5.1 Specifications (SN0011)
- 3.2R. Attachment_ Risk assessment (SN0011)
- 3.2.R Attachment_ Medical Device_ Essential Performance Requirements (SN0011)
- CMC response 10-June 2016 (SN0002) "Documentation as to the presence of the human factor study or rationale explaining why a human factor study might not have been conducted".
- CMC response 14-June 2016- Risk Management Summary Report and User Failure Mode and Effects Analysis
- CMC response 29-June 2016 (SN0007)
- CMC response 29-July 2016 (SN0010)
- CMC response 15-August 2016 (SN0011)
- 3.2.R attachment_ Risk Assessment- (b) (4) Study Report
- Final Report- (b) (4)
- (b) (4)
-
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This review did not cover the following content

- Review of drug product
- Review of primary container closure-drug product interaction, sterility, or toxicology
- Manufacturing of the drug product
- Manufacturing of the device constituent part of the combination product

III. Intended Use

The following intended use was within the Risk Assessment Summary in Module 1.11.1 Quality information amendment under sequence 003:

> *Maraviroc (Selzentry) oral solution has been developed for the treatment of pediatric patients infected with CCR5 tropic HIV-1.*

(b) (4)

IV. Consult Purpose

The Center for Drugs Evaluation and Research (CDER) requested a consult from CDRH/ODE for review of device constituent part design for the combination product submitted under the NDA 208984. CDRH/ODE was consulted to review the device design and performance of the oral syringe and press in bottle adaptor of the combination product.

V. Background

Selzentry (Maraviroc) is a CCR5 co-receptor antagonist indicated for combination antiretroviral treatment of adults infected with only CCR5-tropic HIV-1.

The NDA 022128 for Selzentry (Maraviroc) tablets was originally approved on August 6, 2007. ViiV Healthcare is simultaneously submitting two applications supporting expansion of the intended use of Selzentry to include patients 2 years of age and older and weighing at least 10 kg. In addition to updating the approved product labeling, ViiV Healthcare also seeks approval of age appropriate dosage forms in order to facilitate dosing in children and adolescents. The supplemental NDA (NDA 22128; seq 340) is seeking approval of two lower strength tables. The current NDA 208984 contains data that addresses an outstanding PREA study requirement.

This original application also includes Chemistry, Manufacturing, and Controls information supporting the new oral solution (20 mg/ml) dosage form and a dispensing device (10 ml oral syringe) to be packaged with the new formulation. The NDA contains information supporting the performance of the device constituent parts, including descriptive information and test data for the press-in bottle adapter and 10 ml syringe.

INDICATIONS AND USAGE
SELZENTRY is a CCR5 co-receptor antagonist indicated in combination with other antiretroviral agents for the treatment of CCR5-tropic HIV-1 infection.

- Tropism testing with a highly sensitive tropism assay (b) (4) (b) (4).

DOSAGE AND ADMINISTRATION

Adults

When given with potent CYP3A inhibitors (with or without potent CYP3A inducers) including PIs (except tipranavir/ritonavir), delavirdine (2 [(b) (4)] 7.1)	150 mg twice daily
With NRTIs, tipranavir/ritonavir, nevirapine, raltegravir, and other drugs that are not potent CYP3A inhibitors or CYP3A inducers (2 [(b) (4)] 7.1)	300 mg twice daily
With potent CYP3A inducers including efavirenz (without a potent CYP3A inhibitor) (2 [(b) (4)] 7.1)	600 mg twice daily

A more complete list of coadministered drugs is listed in *Dosage and Administration (2)*.

Pediatric Patients Aged 2 Years and Older and Weighing at Least 10 kg: Administer twice daily. [(b) (4)] should be based on body weight (kg) and concomitant medications and should not exceed the recommended adult dose.

Patients with Renal Impairment: Dose adjustment may be necessary in patients with renal impairment.

Dosage Forms and Strengths

Tablets: 25 mg, 75 mg, 150 mg, and 300 mg
Oral Solution: 20 mg per mL

VI. Device Description

Components

10 ml, oral dosing syringe
Press-in bottle adaptor

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(b) (4)

The sponsor has responded to all the sent IR. All deficiencies have been resolved.

VIII. Concurrence Table

Digital Signature Concurrence Table	
Reviewer Sign-Off	Sarah B. Mollo -S Digitally signed by Sarah B. Mollo -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Sarah B. Mollo -S, 0.9.2342.19200300.100.1.1=2001712033 Date: 2016.10.05 13:40:19 -04'00'
Branch Sign-Off	Alan M. Stevens -S Digitally signed by Alan M. Stevens -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300189211, cn=Alan M. Stevens -S Date: 2016.10.05 14:55:24 -04'00'

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/s/

BAMIDELE F AISIDA
10/06/2016

Erika Pfeiler

Digitally signed by Erika Pfeiler
Date: 10/04/2016 01 32:32PM
GUID: 502d1da500002b6a73a00c0e0dff6e1d

John Arigo

Digitally signed by John Arigo
Date: 10/05/2016 07 34:28AM
GUID: 508da70b00028eb5ce7d95d2ab482661

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance, Division of Manufacturing & Quality
Physical Medicine, Orthopedic, Neurology, and Dental Devices Branch

Date: August 11, 2016

To: Steve Miller
CDER/OPQ/ONDP/DNDPI/NDPBIII
W.O. 22-1446
stephen.miller@fda.hhs.gov

Office of combination products at combination@fda.gov

RPM: Bamidele (Florence) Aisida
bamidele.aisida@fda.hhs.gov

Through: Matthew Krueger, Chief, POND/DMQ/OC/CDRH

From: Katelyn R. Bittleman, CSO, POND/DMQ/OC/CDRH

Applicant: ViiV Healthcare Company
5 Moore Drive
Research Triangle Park, North Carolina, 27709
FEI#: 3008108109

Application # NDA 208984

Consult # ICC1600387

Product Name: Maraviroc (Selzentry®)

Pre-Approval Inspection: No

Documentation Review: No Additional Information Required

Final Recommendation: **No Review Needed**

The Office of Compliance at CDRH received a consult request from CDER to evaluate the applicant's compliance with applicable Quality System Requirements for the approvability of NDA 208984.

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/s/

BAMIDELE F AISIDA
10/03/2016

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/s/

JONATHAN T DOW
11/09/2016

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	August 10, 2016
Requesting Office or Division:	Division of Antiviral Products (DAVP)
Application Type and Number:	NDA 22128/S-17 and NDA 208984
Product Name and Strength:	Selzentry (maraviroc), Oral Solution and Tablets 20 mg/mL and 25 mg, 75 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Viiv Healthcare
Submission Date:	May 6, 2016
OSE RCM #:	2016-1286 and 2016-1287
DMEPA Primary Reviewer:	Mónica Calderón, PharmD, BCPS
DMEPA Team Leader:	Vicky Borders-Hemphill, PharmD

1 REASON FOR REVIEW

Viiv Healthcare submitted two applications for the expansion of the intended use of Selzentry to include patients 2 years of age and older and weighing at least 10 kg.

1. NDA 208984 seeks approval of a new oral solution dosage form (20 mg/mL) addressing an outstanding PREA requirement and provides partial response to a FDA Pediatric Written Request.
2. Supplemental NDA 22128 (S-17) seeks approval of labeling changes and two lower strength tablets (25 mg and 75 mg).

Thus, the Division of Antiviral Products (DAVP) requested DMEPA evaluate the Applicant's proposed full prescribing information (FPI), Medication Guide, Instructions for Use (IFU), container labels and carton labeling, and packaging configuration.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	C (N/A)
ISMP Newsletters	D
FDA Adverse Event Reporting System (FAERS)*	E
Other	F (N/A)
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS for label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Selzentry (maraviroc) oral tablets (150 mg and 300 mg) were approved August 6, 2007 under NDA 22128. Viiv Healthcare submitted NDA 208984 seeking approval of a new oral solution dosage form (20 mg/mL) to facilitate dosing in children and adolescents and includes co-packaged press-in bottle adapter and 10 ml oral syringe. Viiv Healthcare submitted supplemental NDA (sNDA 22128/S-17) to add two lower strength oral tablets (25 mg and 75 mg). We performed a risk assessment of the revised shared full prescribing information (FPI), Medication Guide, Instructions for Use (IFU), container labels and carton labeling, and packaging configuration to identify deficiencies that may lead to medication errors and areas of

improvement. We determined that the proposed oral solution and new tablet strengths will require label and labeling changes prior to being introduced to the market.

FAERS cases

DMEPA conducted a FAERS search and determined that the results did not inform our review of the proposed labels and labeling (see Appendix E).

Container Label and Carton Labeling

The container label for the proposed oral solution does not include a barcode. The Sponsor has used different colors to help differentiate between the tablet strengths; however, the color of the container label for the oral solution is similar to the color used for the marketed 300 mg tablets. We provide recommendations to include required barcode information and to revise the color scheme to prevent product selection errors between the oral solution and tablet. Also, as presented, the oral solution carton lists the contents on the PDP; however, we provide recommendations to use clarifying terminology to read "1 oral dosing syringe" and "1 press-in bottle adapter" (See Sections 4.1 and 4.2.)

Full Prescribing Information (FPI)

The revised Highlights, Dosage and Administration section, Dosage Forms section, and Storage and Handling section have been updated to reflect the proposal for the new tablets and oral solutions dosage forms and the new pediatric indication. We noted the use of error prone symbols within the tables in Section 2 (Dosage and Administration) to indicate greater than, less than, etc. and have provided recommendations in Section 3.1 to provide clarification and improve readability within the tables.

Medication Guide

The Medication Guide has been updated to reflect the new dosage forms and indication for pediatric patients. The information is clearly stated and we have no risk mitigation strategies to recommend at this time.

IFU

The IFU provides step-by-step instructions addressing how to place the adapter in the bottle and how to draw up the solution. The instructions include graphics to assist the user; however, we noted there are no references to indicate which graphics coincide with which instructions. Also, some instructions may be better understood with additional graphics. We provide recommendations in Section 3.2 to improve readability. We shared our recommendations with The Division of Medication Policy Programs (DMPP) and we defer to DMPP for further recommendations.

Oral dosing syringe

The Sponsor submitted an illustrative representation of the oral syringe (Appendix G) under IND 65229 in response to our Preliminary comments in the Type B Meeting Package.[1] The revisions

[1] IND 65229 Meeting Preliminary Comments. July 14, 2015; 2015-1017.

implemented our recommendations and we have no additional recommendations at this time. Also of note, the oral dosing syringe is 10 mL and the highest dose given with the oral solution will be 300 mg (15 mL). The oral dosing syringe supplied is 10 mL and will require caregivers and/or patients to divide the dose. Due to the lowest dose needed, i.e 2.5 mL, the 10 mL oral syringe is appropriate for the dosing range. The instructions for use (b) (4) address the need to divide the dose adequately.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes the proposed FPI, Medication Guide, IFU, container labels and carton labeling and packaging configuration are acceptable. However, to provide clarity, improve readability, and minimize the potential for strength selection errors, we provide recommendations in Section 4.1 and 4.2. We advise the recommendations below are implemented prior to approval of this application and the supplement.

4.1 RECOMMENDATIONS FOR THE DIVISION

Full Prescribing Information

1. We noted the use of error prone symbols within the tables in Section 2 (Dosage and Administration) to indicate greater than, less than, etc. We provide recommended revisions to the Division's working FPI document (see Appendix G) to revise the D&A section.

Instructions for Use

1. The instructions include graphics to assist the user; however, we noted there are no references to indicate which graphics coincide with which instructions. Also, some instructions may be better understood with additional graphics. We provide recommended revisions to the Division's working FPI document (see Appendix G) to revise the IFU.
2. We shared our recommendations with and defer to the Division of Medication Policy Programs (DMPP) for further recommendations.

4.2 RECOMMENDATIONS FOR VIIV HEALTHCARE

Container Label and Carton Labeling For Oral Solution

1. As presented, the labels and labeling for the oral solution and the marketed 300 mg tablet strength are similar in color. Revise the colored box for the strength of the oral solution to a dissimilar color to help differentiate the labels and labeling to prevent strength selection errors.

Carton Labeling For Oral Solution

1. As presented, the carton lists the contents of the carton on the PDP; however we recommend to use clarifying terminology. Revise the following contents, (b) (4) (b) (4) to read "1 oral dosing syringe" and (b) (4) to read, "1 press-in bottle adapter".

Container Label For Oral Solution

1. Per 21 CFR 201.25(c)(2), place the barcode on the immediate container.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Selzentry that Viiv Healthcare submitted on May 6, 2016.

Table 2. Relevant Product Information for Selzentry

Initial Approval Date	Aug 6, 2007
Active Ingredient	maraviroc
Indication	In combination with other antiretroviral agents for adult patients infected with only CCR-5 tropic HIV-1 Proposed: in combination with other antiretroviral agents for the treatment of CCR-5 tropic HIV-1 infection
Route of Administration	Oral
Dosage Form	Tablet Proposed: oral solution
Strength	150 mg and 300 mg Proposed: 25 mg, 75 mg, and 20 mg/mL
Dose and Frequency	Adults (2 (b) (4) When given with potent CYP3A inhibitors (with or without potent CYP3A inducers) including PIs (except tipranavir/ritonavir), delavirdine (2 (b) (4) 7.1) — 150 mg twice daily With NRTIs, tipranavir/ritonavir, nevirapine, raltegravir, and other drugs that are not potent CYP3A inhibitors or CYP3A inducers (2 (b) (4) 7.1) — 300 mg twice daily With potent CYP3A inducers including efavirenz (without a potent CYP3A inhibitor) (2 (b) (4) 7.1) — 600 mg twice daily Proposed: Pediatric Patients Aged 2 Years and Older and Weighing at Least 10 kg: Administer twice daily. Dose should be based on body weight (kg) and concomitant medications and should not exceed the recommended adult dose. Table 2. Recommended (b) (4) in Pediatric Patients Aged 2 Years and Older (Tablets) Dose of SELZENTRY Based on Weight Concomitant Medications | 10 kg - <20 kg | 20 kg - <30 kg | 30 kg - <40 kg | ≥40 kg Potent CYP3A inhibitors (with or without a CYP3A inducer (b) (4) | 50 mg twice daily | 75 mg twice daily | 100 mg twice daily | 150 mg twice daily (b) (4) concomitant medications (b) (4) (b) (4) Potent CYP3A inducers (without a potent CYP3A inhibitor (b) (4) (b) (4)

	Table 3. Recommended [redacted] in Pediatric Patients Aged 2 Years and Older (Oral Solution) [redacted] of SELZENTRY Based on Weight Concomitant Medications: 10 kg - <20 kg; 20 kg - <30 kg; 30 kg - <40 kg; ≥40 kg Potent CYP3A inhibitors (with or without a CYP3A inducer [redacted]): 50 mg (2.5 mL) twice daily; 80 mg (4 mL) twice daily; 100 mg (5 mL) twice daily; 150 mg (7.5 mL) twice daily [redacted] concomitant medications[a]: [redacted] Potent CYP3A inducers (without a potent CYP3A inhibitor [redacted]): [redacted]
How Supplied	150 mg tablets: bottle of 60 tablets 300 mg tablets: bottle of 60 tablets Proposed: 25 mg tablets: bottle of 120 tablets 75 mg tablets: bottle of 120 tablets 20 mg/mL oral solution: bottle of [redacted] mL packaged with a press-in [redacted] adaptor and a 10 mL oral dosing syringe with 0.5 mL gradations
Storage	25°C (77°F)

B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On July 5, 2016, we searched the L:drive and AIMS using the terms, Selzentry to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified 2 previous reviews[2,3], and we confirmed that our previous recommendations were implemented.

[2] IND 65229 Meeting Preliminary Comments. July 14, 2015; 2015-1017.

[3] Toyer D. Consultation Maraviroc NDA 22128. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2006 12 06. RCM No.: 2007-245.

APPENDIX D. ISMP NEWSLETTERS

D.1 Methods

On July 5, 2016, we searched the Institute for Safe Medication Practices (ISMP) newsletters using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newletter(s)	Acute Care Nursing Community
Search Strategy and Terms	Match Exact Word or Phrase: Selzentry

D.2 Results

No cases were identified.

APPENDIX E. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

E.1 Methods

We searched the FDA Adverse Event Reporting System (FAERS) on July 5, 2016 using the criteria in Table 3, and then individually reviewed each case. We limited our analysis to cases that described errors possibly associated with the label and labeling. We used the NCC MERP Taxonomy of Medication Errors to code the type and factors contributing to the errors when sufficient information was provided by the reporter.[4]

Table 3: FAERS Search Strategy	
Date Range	**July 5, 2016**
Product	**MARAVIROC** [active ingredient] **SELZENTRY** [product name]
Event (MedDRA Terms)	**DMEPA Official FBIS Search Terms Event List:** Contraindicated Drug Administered (PT) Drug Administered to Patient of Inappropriate Age (PT) Inadequate Aseptic Technique in Use of Product (PT) Medication Errors (HLGT) Overdose (PT) Prescribed Overdose (PT) Prescribed Underdose (PT) Product Adhesion Issue (PT) Product Compounding Quality Issue (PT) Product Formulation Issue (PT) Product Label Issues (HLT) Product Packaging Issues (HLT) Product Use Issue (PT) Underdose (PT)

E.2 Results

Our search identified 15 cases, of which 2 described errors relevant for this review.

- Improper dose (n=2)
  We identified two improper dose medication error cases. One case involved off label dosing of 300 mg once daily. No adverse events were reported and no root cause could be determined. The second case involved a dispensing error. The physician prescribed

[4] The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Taxonomy of Medication Errors. Website http://www.nccmerp.org/pdf/taxo2001-07-31.pdf.

150 mg twice daily; however, the ADAP nurse dispensed 300 mg twice daily. No AE's reported and no root cause could be determined. The Dosage and Administration section of the FPI and the "How should I take Selzentry" section of the Medication Guide clearly state the dosage and frequency of the medication.

We excluded 13 cases because they described:

- Adverse events unrelated to medication errors (n=6)
- Adverse events unrelated to Selzentry (n=2)
- Overdose death unrelated to Selzentry (n=2)
- Medication error unrelated to Selzentry (n=2)
- Insufficient information to determine if a medication error occurred (n=1)

E.3 List of FAERS Case Numbers

Below is a list of the FAERS case number and manufacturer control numbers for the cases relevant for this review.

Case number	Case version	Manufacturer Control Number	
10475320	1	US-VIIV HEALTHCARE LIMITED-A1045056A	"This case was reported by a healthcare professional and described the occurrence of maladministration in a patient who received Maraviroc (Selzentry) for human immunodeficiency virus. On an unknown date, the patient started Maraviroc (oral), unknown dosing. At an unknown time after starting Maraviroc, the patient experienced maladministration. A medical scientist reported that there is a prescriber who is prescribing the medication for HIV, at a different dose than what is recommended in the prescribing information. The reporter stated that there were good results,the patient is improving and is tolerating it very well .Follow-up information from the medical scientist was received on 10 January 2014. The patient did not experience an adverse event, but experienced off label dosing. The patient was treated with Maraviroc

			300 mg daily, which was off label dosage and not an approved dosing interval. Treatment with Maraviroc was continued."
10475326	1	US-VIIV HEALTHCARE LIMITED-A1051748A	"This case was reported by a nurse, via a sales representative, and described the occurrence of no adverse drug effect in a patient who received Maraviroc (Selzentry) film-coated tablet for an unknown drug indication. Medical history and concurrent treatment were not provided. On an unknown date, the patient started Maraviroc (unknown). The prescribed dose was 150 mg twice daily for a total daily dose of 300 mg. But, the ADAP nurse wrongly dispensed 300 mg twice daily to the patient (dispensing error). The patient noticed the error and self-corrected by taking 300 mg once daily (wrong dose administered). After about a month at this regimen, the clinic found out about the mistake and the dosing regimen was corrected. Unspecified laboratory testing showed that the patient was ""OK"", and the patient was doing well as of the time of the report (no adverse drug effect)."

E.4 Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

APPENDIX F. Type B Pre-NDA Meeting Preliminary Comments July 14, 2015 (IND 65229)

F.1 Methods

On July 14, 2015, DMEPA provided preliminary comments to the Applicant indicating their proposed dispensing device is not appropriate.[5] It was recommended the Applicant use only one unit of measure (metric) on the dispensing device, (b) (4) (b) (4) (b) (4)

F.2 Results

The Sponsor submitted a response to our preliminary comments and implemented the changes requested (Appendix G) with the exception of adding the statement (b) (4) (b) (4)

We find their rationale acceptable. We also note the following statement "SELZENTRY oral solution should be given with the supplied oral dosing syringe" is included in the Medication Guide (b) (4) (b) (4)

[5] IND 65229 Meeting Preliminary Comments. July 14, 2015; 2015-1017.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[6] along with postmarket medication error data, we reviewed the following Selzentry labels and labeling submitted by Viiv Healtchare on May 6, 2016.

- Container label
- Carton labeling
- FPI (Dosage and Administration section)
- Instructions for Use

G.2 Label and Labeling Images

(b) (4)

[6] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

MONICA M CALDERON
08/10/2016

BRENDA V BORDERS-HEMPHILL
08/10/2016

REGULATORY PROJECT MANAGER
PHYSICIAN LABELING RULE (PLR) FORMAT REVIEW
OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: NDA 208984

Application Type: NDA

Drug Name(s)/Dosage Form(s): SELZENTRY (maraviroc)

Applicant: ViiV Healthcare Company

Receipt Date: May 6, 2016

Goal Date: November 6, 2016

1. Regulatory History and Applicant's Main Proposals

Viiv Healthcare Company. submitted an NDA to expand the patient population to include pediatric patients. This application was submitted simultaneously with NDA 22128/S-17, a supplemental NDA proposing two new lower strength tablets. The original NDA and supplemental NDA for Selzentry proposes to expand the patients ages 2 to less than 18 years of age. NDA 22-128/S17 supports two new tablet strengths, 25 mg and 75 mg and NDA 208984 supports a new oral formulation.

This application is a response to PREA PMR 1357-2, "Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from 2 to 18 years of age. This study will determine the maraviroc exposure (pharmacokinetics profile) followed by 48 weeks of dosing, with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from 2 to 18 years of age to support maraviroc dose selection, safety and efficacy". In addition, this application is a partial response to a written request for maraviroc.

The clinical data required to support the two new tablet strengths were submitted to NDA 208984 and a letter of cross reference was included to this sNDA. Included in this sNDA are the required regulatory documents in Module 1 and CMC information to support the two new tablet strengths.

At the filing meeting, the review team decided this application will be reviewed under a 6 month, priority review clock.

2. Review of the Prescribing Information

This review is based on the applicant's submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements of Prescribing Information (SRPI)" checklist (see Section 4 of this review).

3. Conclusions/Recommendations

No SRPI format deficiencies were identified in the review of this PI.

4. Selected Requirements of Prescribing Information

The Selected Requirement of Prescribing Information (SRPI) is a 41-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

YES 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

Comment:

YES 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement. Instructions to complete this item: If the length of the HL is one-half page or less, select "YES" in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select "NO" unless a waiver has been granted.

Comment:

YES 3. A horizontal line must separate:
- HL from the Table of Contents (TOC), **and**
- TOC from the Full Prescribing Information (FPI).

Comment:

YES 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be **bolded** and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format.

Comment:

YES 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix for HL format.

Comment:

YES 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

Comment:

YES 7. Headings in HL must be presented in the following order:

Heading	Required/Optional
• **Highlights Heading**	Required

Selected Requirements of Prescribing Information

• **Highlights Limitation Statement**	Required
• **Product Title**	Required
• **Initial U.S. Approval**	Required
• **Boxed Warning**	Required if a BOXED WARNING is in the FPI
• **Recent Major Changes**	Required for only certain changes to PI*
• **Indications and Usage**	Required
• **Dosage and Administration**	Required
• **Dosage Forms and Strengths**	Required
• **Contraindications**	Required (if no contraindications must state "None.")
• **Warnings and Precautions**	Not required by regulation, but should be present
• **Adverse Reactions**	Required
• **Drug Interactions**	Optional
• **Use in Specific Populations**	Optional
• **Patient Counseling Information Statement**	Required
• **Revision Date**	Required

* RMC only applies to five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment: *Directed to see 17 for patient counseling information and medication guide*

HIGHLIGHTS DETAILS

Highlights Heading

YES 8. At the beginning of HL, the following heading, **"HIGHLIGHTS OF PRESCRIBING INFORMATION"** must be **bolded** and should appear in all UPPER CASE letters.

Comment:

Highlights Limitation Statement

YES 9. The **bolded** HL Limitation Statement must include the following verbatim statement: "**These highlights do not include all the information needed to use (insert NAME OF DRUG PRODUCT) safely and effectively. See full prescribing information for (insert NAME OF DRUG PRODUCT).**" The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

YES 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

YES 11. Initial U.S. Approval must be **bolded**, and include the verbatim statement "**Initial U.S. Approval:**" followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

YES 12. All text in the BW must be **bolded**.

Comment:

YES 13. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. Even if there is more than one warning, the term

"**WARNING**" and not "**WARNINGS**" should be used. For example: "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings. The BW title should be centered.

Comment:

YES 14. The BW must always have the verbatim statement "***See full prescribing information for complete boxed warning***." This statement must be placed immediately beneath the BW title, and should be centered and appear in *italics*.

Comment:

YES 15. The BW must be limited in length to 20 lines. (This includes white space but does not include the BW title and the statement "***See full prescribing information for complete boxed warning.***")

Comment:

Recent Major Changes (RMC) in Highlights

YES 16. RMC pertains to only five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the FPI.

Comment:

YES 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section's identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, "Warnings and Precautions, Acute Liver Failure (5.1) --- 8/2015."

Comment: *Noted, in xx/xxxx format currently*

NO 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

Comment: *??*

Dosage Forms and Strengths in Highlights

YES 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

Comment:

Contraindications in Highlights

YES 20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word "None."

Comment:

Selected Requirements of Prescribing Information

Adverse Reactions in Highlights

YES 21. For drug products other than vaccines, the verbatim **bolded** statement must be present: "**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer's U.S. phone number which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**"

Comment:

Patient Counseling Information Statement in Highlights

YES 22. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- **See 17 for PATIENT COUNSELING INFORMATION**

If a product **has (or will have)** FDA-approved patient labeling:

- **See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**
- **See 17 for PATIENT COUNSELING INFORMATION and Medication Guide**

Comment:

Revision Date in Highlights

YES 23. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., "**Revised: 8/2015** ").

Comment:

Contents: Table of Contents (TOC)

See Appendix for a sample tool illustrating Table of Contents format.

YES 24. The TOC should be in a two-column format.

Comment:

YES 25. The following heading must appear at the beginning of the TOC: **"FULL PRESCRIBING INFORMATION: CONTENTS."** This heading should be in all UPPER CASE letters and **bolded**.

Comment:

YES 26. The same title for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.

Comment:

YES 27. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.

Comment:

YES 28. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (for, of, to) and articles (a, an, the), or conjunctions (or, and)].

Comment:

YES 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading "**FULL PRESCRIBING INFORMATION: CONTENTS***" must be followed by an asterisk and the following statement must appear at the end of the TOC: "*Sections or subsections omitted from the full prescribing information are not listed."

Comment:

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

YES 31. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. (Section and subsection headings should be in UPPER CASE and title case, respectively.) If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use "**Labor and Delivery**")
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use "**Nursing Mothers**")
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

YES 32. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, *"[see Warnings and Precautions (5.2)]."*

Comment: *Need to follow-up with LO*

YES

33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

YES 34. The following heading "**FULL PRESCRIBING INFORMATION"** must be **bolded,** must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

YES 35. All text in the BW should be **bolded**.

Comment:

YES 36. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. (Even if there is more than one warning, the term, "**WARNING**" and not "**WARNINGS**" should be used.) For example: "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings.

Comment:

CONTRAINDICATIONS Section in the FPI

YES 37. If no Contraindications are known, this section must state "None."

Comment:

ADVERSE REACTIONS Section in the FPI

YES 38. When clinical trials adverse reactions data are included (typically in the "Clinical Trials Experience" subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

"Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice."

Comment:

YES 39. When postmarketing adverse reaction data are included (typically in the "Postmarketing Experience" subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions:

"The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure."

Comment:

PATIENT COUNSELING INFORMATION Section in the FPI

YES 40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment:

YES 41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) must not be included as a subsection under Section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Appendix: Highlights and Table of Contents Format

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.

- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)

Limitations of Use: Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

Revised: M/201Y

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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

/s/

LINDA C ONAGA
07/01/2016

KAREN D WINESTOCK
07/01/2016

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

/s/

LINDA C ONAGA
06/30/2016

KAREN D WINESTOCK
06/30/2016

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

<table>
<tr><th colspan="3">Application Information</th></tr>
<tr><td>NDA # 208984</td><td></td><td>Efficacy Supplement Category:
☐ New Indication (SE1)
☐ New Dosing Regimen (SE2)
☐ New Route Of Administration (SE3)
☐ Comparative Efficacy Claim (SE4)
☐ New Patient Population (SE5)
☐ Rx To OTC Switch (SE6)
☐ Accelerated Approval Confirmatory Study (SE7)
☐ Labeling Change With Clinical Data (SE8)
☐ Manufacturing Change With Clinical Data (SE9)
☐ Animal Rule Confirmatory Study (SE10)</td></tr>
<tr><td colspan="3">Proprietary Name: Selzentry
Established/Proper Name: maraviroc
Dosage Form: Oral Solution
Strengths: 20mg/ml</td></tr>
<tr><td colspan="3">Applicant: Viiv Healthcare
Agent for Applicant (if applicable): Mark Baumgartner, Sr. Director, Global Regulatory Affairs, GlazoSmithKline</td></tr>
<tr><td colspan="3">Date of Application: May 6, 2016
Date of Receipt: May 6, 2016
Date clock started after Unacceptable for Filing (UN):</td></tr>
<tr><td colspan="2">PDUFA/BsUFA Goal Date:
November 6, 2016</td><td>Action Goal Date (if different):
November 4, 2016</td></tr>
<tr><td colspan="2">Filing Date: July 5, 2016</td><td>Date of Filing Meeting: May 31, 2016</td></tr>
<tr><td colspan="3">Chemical Classification (original NDAs only) :
☐ Type 1- New Molecular Entity (NME); NME and New Combination
☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination
☒ Type 3- New Dosage Form; New Dosage Form and New Combination
☐ Type 4- New Combination
☐ Type 5- New Formulation or New Manufacturer
☐ Type 7- Drug Already Marketed without Approved NDA
☐ Type 8- Partial Rx to OTC Switch
☐ Type 9-New Indication or Claim (will not be marketed as a separate NDA after approval)
☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)</td></tr>
<tr><td colspan="3">Proposed indication(s)/Proposed change(s): Original NDA proposes to expand the patient population to include pediatric subjects from ≥ 2 to less than 18 years of age.</td></tr>
<tr><td colspan="2">Type of Original NDA:
AND (if applicable)
Type of NDA Supplement:

If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment”</td><td>☒ 505(b)(1)
☐ 505(b)(2)
☒ 505(b)(1)
☐ 505(b)(2)</td></tr>
</table>

review found at: ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499.***	

Type of BLA ***If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team***	☐ 351(a) ☐ 351(k)
Review Classification: ***The application will be a priority review if:*** • ***A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)*** • ***The product is a Qualified Infectious Disease Product (QIDP)*** • ***A Tropical Disease Priority Review Voucher was submitted*** • ***A Pediatric Rare Disease Priority Review Voucher was submitted***	☐ Standard ☒ Priority ☐ Pediatric WR ☐ QIDP ☐ Tropical Disease Priority Review Voucher ☐ Pediatric Rare Disease Priority Review Voucher
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐
Part 3 Combination Product? ☒ ***If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults***	☒ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling ☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)

☐ Fast Track Designation ☐ Breakthrough Therapy Designation ***(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)*** ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☐ Direct-to-OTC Other:	☐ PMC response ☒ PMR response: ☐ FDAAA [505(o)] ☒ PREA deferred pediatric studies (FDCA Section 505B) ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
Collaborative Review Division (*if OTC product*):	
List referenced IND Number(s): 065229	

Goal Dates/Product Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? ***If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	☒	☐		
Are the established/proper and applicant names correct in electronic archive?	☒	☐		

If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into electronic archive.				
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? ***Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:*** ***http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm*** ***If no, ask the document room staff to make the appropriate entries.***	☒	☐	☐	
Application Integrity Policy	**YES**	**NO**	**NA**	**Comment**
Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at:*** ***http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm***	☐	☒		
If yes, explain in comment column.				
If affected by AIP, has OC been notified of the submission? **If yes,** date notified:	☐	☐		
User Fees	**YES**	**NO**	**NA**	**Comment**
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	☒	☐		

User Fee Status ***If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.***	Payment for this application *(check daily email from UserFeeAR@fda.hhs.gov):* ☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required
If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Contact the User Fee Staff. If appropriate, send UN letter.	Payment of other user fees: ☒ Not in arrears ☐ In arrears
User Fee Bundling Policy ***Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:*** ***http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf***	Has the user fee bundling policy been appropriately applied? ***If no, or you are not sure, consult the User Fee Staff.*** ☒ Yes ☐ No

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is the application a 505(b)(2) NDA? *(Check the 356h form, cover letter, and annotated labeling).* **If yes**, answer the bulleted questions below:	☐	☒		
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☐	☐		
• Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [**see 21 CFR 314.54(b)(1)].**	☐	☐		
• Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [**see 21 CFR 314.54(b)(2)]?** ***If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.***	☐	☐		
• Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm*** **If yes**, please list below:	☐	☐		There is no unexpired exclusivity for this product. Patent code U-824 noted on EOB site.

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.

Exclusivity	**YES**	**NO**	**NA**	**Comment**
Does another product (same active moiety) have orphan exclusivity for the same indication? ***Check the Orphan Drug Designations and Approvals list at:*** ***http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm***	☐	☒		
If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness **[see 21 CFR 316.3(b)(13)]**? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy***	☐	☐	☒	
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	☒	☐	☐	

If yes, # years requested: 3 ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*				
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	☐	☒	☐	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? ***If yes, contact the Orange Book Staff (CDER-Orange Book Staff).***	☐	☐	☒	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? ***If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager*** ***Note****: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☐	☐	☒	

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☒ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	**YES**	**NO**	**NA**	**Comment**
If electronic submission, does it follow the eCTD guidance?[1] **If not,** explain (e.g., waiver granted).	☒	☐	☐	
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21	☒	☐		

[1] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf

CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ☒ legible ☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only) **If no**, explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #	☐	☐	☐	

Forms and Certifications

Electronic *forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise,* ***paper*** *forms and certifications with hand-written signatures must be included.*
Forms *include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674);* ***Certifications*** *include: debarment certification, patent certification(s), field copy certification, and pediatric certification.*

Application Form	**YES**	**NO**	**NA**	**Comment**
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? ***If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].***	☒	☐		
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? ***Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*	☒	☐		
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature? ***If yes, ensure that the application is also coded with the***	☒	☐		

supporting document category, "Form 3674." ***If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant***				
Debarment Certification	**YES**	**NO**	**NA**	**Comment**
Is a correctly worded Debarment Certification included with authorized signature? ***Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*** ***Note:*** *Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e.,"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge…"*	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? ***Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*** ***If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.***	☐	☐	☒	
Controlled Substance/Product with Abuse Potential	**YES**	**NO**	**NA**	**Comment**
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? ***If yes,*** *date consult sent to the Controlled Substance Staff:* <u>For non-NMEs</u>: *Date of consult sent to Controlled Substance Staff* :	☐	☐	☒	
Pediatrics	**YES**	**NO**	**NA**	**Comment**
<u>PREA</u> Does the application trigger PREA? ***If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting[2]***	☒	☐		Pediatric assessment was submitted

***Note**: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*				
If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☐	☐	Sponsor submitted PSP upon request by Division on 6-14-16
If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☒	☐	No agreed iPSP
BPCA: Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required[3]***	☐	☒		
Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."***	☐	☐	☒	
REMS	**YES**	**NO**	**NA**	**Comment**
Is a REMS submitted? ***If yes, send consult to OSE/DRISK and notify OC/ OSI/DSC/PMSB via the CDER OSI RMP mailbox***	☐	☒	☐	
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	☒ Package Insert (Prescribing Information)(PI) ☐ Patient Package Insert (PPI) ☒ Instructions for Use (IFU) ☒ Medication Guide (MedGuide) ☒ Carton labeling ☒ Immediate container labels ☐ Diluent labeling ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL	☒	☐		

[2] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm

[3] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm

format? ***If no, request applicant to submit SPL before the filing date.***				
Is the PI submitted in Physician Labeling Rule (PLR) format?[4]	☒	☐		
If PI not submitted in PLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.***	☐	☐	☒	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	☒ ☒	☐ ☐	☐ ☐	 Consult to MCH sent 6/21/16
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.***	☒	☐	☒	
Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	☒	☐	☐	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (*send WORD version if available*)	☒	☐	☐	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	☒	☐	☐	
OTC Labeling	☒ **Not Applicable**			
Check all types of labeling submitted.	☐ Outer carton label ☐ Immediate container label ☐ Blister card ☐ Blister backing label ☐ Consumer Information Leaflet (CIL) ☐ Physician sample			

[4] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576 htm

	☐ Consumer sample ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is electronic content of labeling (COL) submitted? ***If no, request in 74-day letter.***	☐	☐		
Are annotated specifications submitted for all stock keeping units (SKUs)? ***If no, request in 74-day letter.***	☐	☐	☐	
If representative labeling is submitted, are all represented SKUs defined? ***If no, request in 74-day letter.***	☐	☐	☐	
All labeling/packaging sent to OSE/DMEPA?	☐	☐	☐	
Other Consults	**YES**	**NO**	**NA**	**Comment**
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) ***If yes, specify consult(s) and date(s) sent:***	☐	☐	☒	
Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):**	☐	☐		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):** July 14, 2015	☒	☐		Meeting canceled preliminary comments sent July 14, 2015
Any Special Protocol Assessments (SPAs)? **Date(s):**	☐			

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 31, 2016

BACKGROUND: Viiv Healthcare Company. submitted an NDA to expand the patient population to include pediatric patients. This application was submitted simultaneously with NDA 22128/S-17, a supplemental NDA proposing two new lower strength tablets. The original NDA and supplemental NDA for Selzentry proposes to expand the patients ages 2 to less than 18 years of age. NDA 22-128/S17 supports two new tablet strengths, 25 mg and 75 mg and NDA 208984 supports a new oral formulation.

This application is a response to PREA PMR 1357-2, "Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from 2 to 18 years of age. This study will determine the maraviroc exposure (pharmacokinetics profile) followed by 48 weeks of dosing, with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from 2 to 18 years of age to support maraviroc dose selection, safety and efficacy". In addition, this application is a partial response to a written request for maraviroc.

The clinical data required to support the two new tablet strengths were submitted to NDA 208984 and a letter of cross reference was included to this sNDA. Included in this sNDA are the required regulatory documents in Module 1 and CMC information to support the two new tablet strengths.

At the filing meeting, the review team decided this application will be reviewed under a 6 month, priority review clock.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Andrew Gentles	Y
	CPMS/TL:	Karen Winestock Elizabeth Thompson	N Y
Cross-Discipline Team Leader (CDTL)	Kim Struble		Y
Division Director/Deputy	Debra Birnkrant Jeffrey Murray		Y
Office Director/Deputy			
Clinical	Reviewer:	Melisse Baylor	Y

	TL:	Kim Struble	Y
Social Scientist Review (*for OTC products*)	Reviewer:		
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:		
	TL:		
Clinical Microbiology (*for antimicrobial products*)	Reviewer:	Lisa Naeger	Y
	TL:	Jules O'Rear	Y
Clinical Pharmacology	Reviewer:	Jenny Zheng	Y
	TL:	Shirley Seo	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer: TL:	Mario Sampson Jeffry Florian	N N
Biostatistics	Reviewer:		
	TL:		

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Pritam Verma	N
	TL:	Hanan Ghantous	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Steve Miller	Y
	RBPM:	Florence Bamidele	Y
• Drug Substance	Reviewer:		
• Drug Product	Reviewer:		
• Process	Reviewer:		
• Microbiology	Reviewer:		
• Facility	Reviewer:		
• Biopharmaceutics	Reviewer:		
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)			

OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:	Morgan Walker	
	TL:	Barbara Fuller	
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:	Jessica Fox	
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:	TBD	
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
CDRH	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
• Discipline CDRH	Reviewer:	TBD	
	TL:		
Other attendees			
	*For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

The team discussed the review priority and determined that this application would be granted a priority review because it is a partial response to a written request. The need for an OSE consult to review the human factors study to support the use of the dosing syringe was also discussed. In addition, the team was informed that the application includes a drug copackaged with a dosing device and is considered a combination product. As a result, a CDRH consults would be needed.

GENERAL • 505(b)(2) filing issues: o Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? o Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):	☒ Not Applicable ☐ YES ☐ NO ☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ YES ☐ NO
• Electronic Submission comments **List comments**:	☐ Not Applicable ☒ No comments

CLINICAL **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	☐ YES ☒ NO
• Advisory Committee Meeting needed? **Comments**: ***If no, for an NME NDA or original BLA, include the reason. For example:*** o ***this drug/biologic is not the first in its class*** o ***the clinical study design was acceptable*** o ***the application did not raise significant safety or efficacy issues*** o ***the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease***	☐ YES Date if known: ☒ NO ☐ To be determined Reason:
• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☒ Not Applicable ☐ YES ☐ NO
CONTROLLED SUBSTANCE STAFF • Abuse Liability/Potential **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL MICROBIOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter

CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed? Yes, OSIS consult sent 6/1/16	☒ YES ☐ NO
BIOSTATISTICS **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
New Molecular Entity (NDAs only) • Is the product an NME?	 ☐ YES ☒ NO
Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **Comments**:	 ☒ YES ☐ NO ☐ YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? **Comments**:	☐ Not Applicable ☒ YES ☐ NO

<u>Facility/Microbiology Review</u> (BLAs only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
<u>CMC Labeling Review</u> (BLAs only) **Comments**:	☐ Review issues for 74-day letter
APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs) • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days?	☒ N/A ☐ YES ☐ NO ☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☐ YES ☐ NO

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Jeffrey Murray, MD, MPH **Date of Mid-Cycle Meeting** (for NME NDAs/BLAs in "the Program" PDUFA V): **21st Century Review Milestones (see attached)** (listing review milestones in this document is optional): **Comments**:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. Review Issues: ☒ No review issues have been identified for the 74-day letter. ☐ Review issues have been identified for the 74-day letter. Review Classification: ☐ Standard Review ☒ Priority Review
ACTION ITEMS	
☒	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
☐	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☒	If priority review, notify applicant in writing by day 60 (see CST for choices)
☒	Send review issues/no review issues by day 74
☒	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
☐	Update the PDUFA V DARRTS page (for applications in the Program)
☐	Other

Annual review of template by OND ADRAs completed: April 2016

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

/s/

LINDA C ONAGA
07/01/2016

KAREN D WINESTOCK
07/01/2016

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 022128	NDA Supplement #: S- 17	Efficacy Supplement Category: ☐ New Indication (SE1) ☐ New Dosing Regimen (SE2) ☐ New Route Of Administration (SE3) ☐ Comparative Efficacy Claim (SE4) ☒ New Patient Population (SE5) ☐ Rx To OTC Switch (SE6) ☐ Accelerated Approval Confirmatory Study (SE7) ☐ Labeling Change With Clinical Data (SE8) ☐ Manufacturing Change With Clinical Data (SE9) ☐ Animal Rule Confirmatory Study (SE10)
Proprietary Name: Selzentry Established/Proper Name: maraviroc Dosage Form: Tablet Strengths: 25mg, 75mg (proposed) 150mg, 300mg tablet (approved)		
Applicant: Viiv Healthcare Agent for Applicant (if applicable): Mark Baumgartner, Sr. Director, Global Regulatory Affairs, GlaxoSmithKline		
Date of Application: May 6, 2016 Date of Receipt: May 6, 2016 Date clock started after Unacceptable for Filing (UN):		
PDUFA/BsUFA Goal Date: November 6, 2016	Action Goal Date (if different): November 4, 2016	
Filing Date: July 5, 2016	Date of Filing Meeting: May 31, 2016	
Chemical Classification (original NDAs only) : ☐ Type 1- New Molecular Entity (NME); NME and New Combination ☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination ☐ Type 3- New Dosage Form; New Dosage Form and New Combination ☐ Type 4- New Combination ☒ Type 5- New Formulation or New Manufacturer ☐ Type 7- Drug Already Marketed without Approved NDA ☐ Type 8- Partial Rx to OTC Switch ☐ Type 9-New Indication or Claim (will not be marketed as a separate NDA after approval) ☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)		
Proposed indication(s)/Proposed change(s): Viiv Healthcare, Inc (Viiv) proposes to expand the patient population to include pediatric subjects from 2 to less than 18 years of age. This supplemental NDA proposes two new dosage strength tablets, 25 mg and 75 mg.		
Type of Original NDA: AND (if applicable)	☒ 505(b)(1) ☐ 505(b)(2)	

Type of NDA Supplement: ***If 505(b)(2)NDA/NDA Supplement: Draft the "505(b)(2) Assessment" review found at:*** ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499.***	☒ 505(b)(1) ☐ 505(b)(2)

Type of BLA ***If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team***	☐ 351(a) ☐ 351(k)
Review Classification: ***The application will be a priority review if:*** • ***A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)*** • ***The product is a Qualified Infectious Disease Product (QIDP)*** • ***A Tropical Disease Priority Review Voucher was submitted*** • ***A Pediatric Rare Disease Priority Review Voucher was submitted***	☐ Standard ☒ Priority ☐ Pediatric WR ☐ QIDP ☐ Tropical Disease Priority Review Voucher ☐ Pediatric Rare Disease Priority Review Voucher
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐
Part 3 Combination Product? ☐ ***If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults***	☐ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling ☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)

☐ Fast Track Designation ☐ Breakthrough Therapy Designation ***(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)*** ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☐ Direct-to-OTC Other:	☐ PMC response ☒ PMR response: ☐ FDAAA [505(o)] ☒ PREA deferred pediatric studies (FDCA Section 505B) ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
Collaborative Review Division (*if OTC product*):	
List referenced IND Number(s): 065229	

Goal Dates/Product Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? ***If no, ask the document room staff to correct them immediately.***	☒	☐		

These are the dates used for calculating inspection dates.				
Are the established/proper and applicant names correct in electronic archive? ***If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into electronic archive.***	☒	☐		
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? ***Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:*** ***http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm*** ***If no, ask the document room staff to make the appropriate entries.***	☒	☐	☐	
Application Integrity Policy	**YES**	**NO**	**NA**	**Comment**
Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at:*** ***http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm***	☐	☒		
If yes, explain in comment column.				
If affected by AIP, has OC been notified of the submission? **If yes,** date notified:	☐	☐		
User Fees	**YES**	**NO**	**NA**	**Comment**
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	☒	☐		

User Fee Status ***If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.***	Payment for this application *(check daily email from UserFeeAR@fda.hhs.gov):* ☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required
If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Contact the User Fee Staff. If appropriate, send UN letter.	Payment of other user fees: ☒ Not in arrears ☐ In arrears

User Fee Bundling Policy ***Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:*** ***http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf***	Has the user fee bundling policy been appropriately applied? ***If no, or you are not sure, consult the User Fee Staff.*** ☒ Yes ☐ No

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is the application a 505(b)(2) NDA? *(Check the 356h form, cover letter, and annotated labeling).* **If yes**, answer the bulleted questions below:	☐	☒		
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☐	☐		
• Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [**see 21 CFR 314.54(b)(1)].**	☐	☐		
• Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [**see 21 CFR 314.54(b)(2)]?** ***If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.***	☐	☐		
• Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm*** **If yes**, please list below:	☐	☐		

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.

Exclusivity	**YES**	**NO**	**NA**	**Comment**
Does another product (same active moiety) have orphan exclusivity for the same indication? ***Check the Orphan Drug Designations and Approvals list at:*** ***http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm***	☐	☒		
If another product has orphan exclusivity, is the product	☐	☐	☒	

considered to be the same product according to the orphan drug definition of sameness **[see 21 CFR 316.3(b)(13)]**? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy***				
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? **If yes**, # years requested: 3 ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☒	☐	☐	
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	☐	☒	☐	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? ***If yes, contact the Orange Book Staff (CDER-Orange Book Staff).***	☐	☐	☒	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? ***If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager*** ***Note****: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☐	☐	☒	

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☒ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	**YES**	**NO**	**NA**	**Comment**
If electronic submission, does it follow the eCTD	☒	☐	☐	

guidance?[1] **If not,** explain (e.g., waiver granted).				
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21 CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ☒ legible ☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only) **If no**, explain.	☒	☐		
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #	☐	☐	☐	

Forms and Certifications
Electronic *forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise,* ***paper*** *forms and certifications with hand-written signatures must be included.* ***Forms*** *include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674);* ***Certifications*** *include: debarment certification, patent certification(s), field copy certification, and pediatric certification.*

Application Form	**YES**	**NO**	**NA**	**Comment**
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? ***If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].***	☒	☐		
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? ***Forms must be signed by the APPLICANT, not an Agent [see***	☒	☐		

[1] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf

21 CFR 54.2(g)]. ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*				
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature? ***If yes, ensure that the application is also coded with the supporting document category, "Form 3674."*** ***If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant***	☒	☐		
Debarment Certification	**YES**	**NO**	**NA**	**Comment**
Is a correctly worded Debarment Certification included with authorized signature? ***Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*** ***Note:*** *Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e.,"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge…"*	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? ***Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*** ***If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.***	☐	☐	☒	
Controlled Substance/Product with Abuse Potential	**YES**	**NO**	**NA**	**Comment**
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? ***If yes,*** *date consult sent to the Controlled Substance Staff:* <u>For non-NMEs</u>: *Date of consult sent to Controlled Substance Staff* :	☐	☐	☒	

Pediatrics	YES	NO	NA	Comment
PREA Does the application trigger PREA? ***If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting[2]*** ***Note**: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*	☐	☒		Pediatric assessment was submitted
If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☐	☐	
If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☐	☐	
BPCA: Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required[3]***	☐	☒		Partial response
Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."***	☐	☐	☒	
REMS	**YES**	**NO**	**NA**	**Comment**
Is a REMS submitted? ***If yes, send consult to OSE/DRISK and notify OC/ OSI/DSC/PMSB via the CDER OSI RMP mailbox***	☐	☒	☐	
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	☒ Package Insert (Prescribing Information)(PI) ☐ Patient Package Insert (PPI) ☒ Instructions for Use (IFU) (for oral			

[2] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm

[3] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm

	(b) (4) ☒ Medication Guide (MedGuide) ☐ Carton labeling ☒ Immediate container labels ☐ Diluent labeling ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL format? ***If no, request applicant to submit SPL before the filing date.***	☒	☐		
Is the PI submitted in Physician Labeling Rule (PLR) format?[4]	☒	☐		
If PI not submitted in PLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.***	☐	☐	☒	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	☒ ☒	☐ ☐	☐ ☐	 Consult to MCH sent 6/21/16
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.***	☐	☐	☒	
Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	☒	☐	☐	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (*send WORD version if available*)	☒	☐	☐	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	☒	☐	☐	

[4] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576 htm

OTC Labeling	☒ **Not Applicable**			
Check all types of labeling submitted.	☐ Outer carton label ☐ Immediate container label ☐ Blister card ☐ Blister backing label ☐ Consumer Information Leaflet (CIL) ☐ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is electronic content of labeling (COL) submitted? ***If no, request in 74-day letter.***	☐	☐		
Are annotated specifications submitted for all stock keeping units (SKUs)? ***If no, request in 74-day letter.***	☐	☐	☐	
If representative labeling is submitted, are all represented SKUs defined? ***If no, request in 74-day letter.***	☐	☐	☐	
All labeling/packaging sent to OSE/DMEPA?	☐	☐	☐	
Other Consults	**YES**	**NO**	**NA**	**Comment**
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) ***If yes, specify consult(s) and date(s) sent:***	☐	☐	☒	
Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):**	☐	☐		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):** July 14, 2015	☒	☐		Meeting canceled preliminary comments sent July 14, 2015
Any Special Protocol Assessments (SPAs)? **Date(s):**	☐			

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 31, 2016

BACKGROUND: Viiv Healthcare, Inc. submitted a supplemental NDA to expand the patient population to include pediatric patients. This application was submitted simultaneously with NDA 208984, a new formulation of Selzentry. The supplemental NDA and original NDA for Selzentry proposes to expand the patients ages 2 to less than 18 years of age. NDA 22-128/S17 supports two new tablet strengths, 25 mg and 75 mg and NDA 208984 supports a new oral formulation.

This application is a response to PREA PMR 1357-2, "Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from 2 to 18 years of age. This study will determine the maraviroc exposure (pharmacokinetics profile) followed by 48 weeks of dosing, with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from 2 to 18 years of age to support maraviroc dose selection, safety and efficacy". In addition, this application is a partial response to a written request for maraviroc.

The clinical data required to support the two new tablet strengths were submitted to NDA 208984 and a letter of cross reference was included to this sNDA. Included in this sNDA are the required regulatory documents in Module 1 and CMC information to support the two new tablet strengths.

At the filing meeting, the review team decided this application will be reviewed under a 6 month, priority review clock.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Linda C. Onaga	N
	CPMS/TL:	Karen Winestock Elizabeth Thompson	N Y
Cross-Discipline Team Leader (CDTL)	Kim Struble		Y
Division Director/Deputy	Debra Birnkrant Jeffrey Murray		Y
Office Director/Deputy			
Clinical	Reviewer:	Melisse Baylor	Y

	TL:	Kim Struble	Y
Social Scientist Review (*for OTC products*)	Reviewer:		
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:		
	TL:		
Clinical Microbiology (*for antimicrobial products*)	Reviewer:	Lisa Naeger	Y
	TL:	Jules O'Rear	Y
Clinical Pharmacology	Reviewer:	Jenny Zheng	Y
	TL:	Shirley Seo	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer: TL:	Mario Sampson Jeffry Florian	N N
Biostatistics	Reviewer:		
	TL:		

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Pritam Verma	N
	TL:	Hanan Ghantous	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Allan Fenselau	Y
	RBPM:		
• Drug Substance	Reviewer:		
• Drug Product	Reviewer:		
• Process	Reviewer:		
• Microbiology	Reviewer:		
• Facility	Reviewer:		
• Biopharmaceutics	Reviewer:		
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)			
OMP/OMPI/DMPP (MedGuide, PPI,	Reviewer:	Morgan Walker	

IFU)			
	TL:	Barbara Fuller	
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:	Jessica Fox	
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:	TBD	
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
CDRH	Reviewer:		
	TL:		
Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
• Discipline	Reviewer:		
	TL:		
Other attendees			
	*For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

The team discussed the review priority and determined that this application would be granted a priority review because it is a partial response to a written request. The need for an OSE consult to review the human factors study to support the use of the dosing syringe was also discussed. In addition, the team was informed that the application includes a drug copackaged with a dosing device and is considered a combination product. As a result, a CDRH consults would be needed.

GENERAL • 505(b)(2) filing issues: o Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? o Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):	☒ Not Applicable ☐ YES ☐ NO ☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ YES ☐ NO
• Electronic Submission comments **List comments**:	☐ Not Applicable ☒ No comments

CLINICAL **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	☐ YES ☒ NO
• Advisory Committee Meeting needed? **Comments**:	☐ YES Date if known: ☒ NO

If no, for an NME NDA or original BLA, include the reason. For example: o ***this drug/biologic is not the first in its class*** o ***the clinical study design was acceptable*** o ***the application did not raise significant safety or efficacy issues*** o ***the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease***	☐ To be determined Reason:
• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☒ Not Applicable ☐ YES ☐ NO
CONTROLLED SUBSTANCE STAFF • Abuse Liability/Potential **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL MICROBIOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed? Yes, OSIS consult sent 6/1/16	☒ YES ☐ NO
BIOSTATISTICS **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)	☐ Not Applicable ☒ FILE

Comments:	☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
New Molecular Entity (NDAs only) • Is the product an NME?	☐ YES ☒ NO
Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **Comments**:	☒ YES ☐ NO ☐ YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? **Comments**:	☐ Not Applicable ☒ YES ☐ NO
Facility/Microbiology Review (BLAs only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review (BLAs only) **Comments**:	☐ Review issues for 74-day letter

APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)	☒ N/A
• Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application?	☐ YES ☐ NO
• If so, were the late submission components all submitted within 30 days?	☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☐ YES ☐ NO

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Jeffrey Murray, MD, MPH **Date of Mid-Cycle Meeting** (for NME NDAs/BLAs in "the Program" PDUFA V): **21st Century Review Milestones (see attached)** (listing review milestones in this document is optional): **Comments**:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. Review Issues: ☒ No review issues have been identified for the 74-day letter. ☐ Review issues have been identified for the 74-day letter. Review Classification: ☐ Standard Review ☒ Priority Review
ACTION ITEMS	
☒	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
☐	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☒	If priority review, notify applicant in writing by day 60 (see CST for choices)
☒	Send review issues/no review issues by day 74
☒	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
☐	Update the PDUFA V DARRTS page (for applications in the Program)
☐	Other

Annual review of template by OND ADRAs completed: April 2016

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

/s/

LINDA C ONAGA
07/01/2016

KAREN D WINESTOCK
07/01/2016

REGULATORY PROJECT MANAGER
PHYSICIAN LABELING RULE (PLR) FORMAT REVIEW
OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: NDA 022128/S-017

Application Type: supplemental NDA, Type 5 (new formulation)

Drug Name(s)/Dosage Form(s): SELZENTRY (maraviroc)

Applicant: ViiV Healthcare

Receipt Date: May 6, 2016

Goal Date: November 6, 2016

1. Regulatory History and Applicant's Main Proposals

Viiv Healthcare, Inc. submitted a supplemental NDA and a New NDA to expand the patient population to include pediatric patients 2 to less than 18 years of age. NDA 22-128/S17 supports two new tablet strengths, 25 mg and 75 mg and NDA 208984 supports a new oral formulation.

This application is a response to PREA PMR 1357-2, "Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from 2 to 18 years of age. This study will determine the maraviroc exposure (pharmacokinetics profile) followed by 48 weeks of dosing, with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from 2 to 18 years of age to support maraviroc dose selection, safety and efficacy". In addition, this application is a partial response to a Written Request for maraviroc.

The clinical data required to support the two new tablet strengths were submitted to NDA 208984 and a letter of cross reference was included to this sNDA. Included in this sNDA are the required regulatory documents in Module 1 and chemistry manufacturing and controls, information to support the two new tablet strengths.

2. Review of the Prescribing Information

This review is based on the applicant's submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements of Prescribing Information (SRPI)" checklist (see Section 4 of this review).

3. Conclusions/Recommendations

No SRPI format deficiencies were identified in the review of this PI.

4. Selected Requirements of Prescribing Information

The Selected Requirement of Prescribing Information (SRPI) is a 41-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

YES 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

Comment:

YES 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement. Instructions to complete this item: If the length of the HL is one-half page or less, select "YES" in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select "NO" unless a waiver has been granted.

Comment:

YES 3. A horizontal line must separate:

- HL from the Table of Contents (TOC), **and**
- TOC from the Full Prescribing Information (FPI).

Comment:

YES 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be **bolded** and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format.

Comment:

YES 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix for HL format.

Comment:

YES 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

Comment:

YES 7. Headings in HL must be presented in the following order:

Heading	Required/Optional
• **Highlights Heading**	Required
• **Highlights Limitation Statement**	Required

Selected Requirements of Prescribing Information

• **Product Title**	Required
• **Initial U.S. Approval**	Required
• **Boxed Warning**	Required if a BOXED WARNING is in the FPI
• **Recent Major Changes**	Required for only certain changes to PI*
• **Indications and Usage**	Required
• **Dosage and Administration**	Required
• **Dosage Forms and Strengths**	Required
• **Contraindications**	Required (if no contraindications must state "None.")
• **Warnings and Precautions**	Not required by regulation, but should be present
• **Adverse Reactions**	Required
• **Drug Interactions**	Optional
• **Use in Specific Populations**	Optional
• **Patient Counseling Information Statement**	Required
• **Revision Date**	Required

* RMC only applies to five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment: *Directed to see 17 for patient counseling information and medication guide*

HIGHLIGHTS DETAILS

Highlights Heading

YES 8. At the beginning of HL, the following heading, **"HIGHLIGHTS OF PRESCRIBING INFORMATION"** must be **bolded** and should appear in all UPPER CASE letters.
Comment:

Highlights Limitation Statement

YES 9. The **bolded** HL Limitation Statement must include the following verbatim statement: "**These highlights do not include all the information needed to use (insert NAME OF DRUG PRODUCT) safely and effectively. See full prescribing information for (insert NAME OF DRUG PRODUCT).**" The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

YES 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

YES 11. Initial U.S. Approval must be **bolded**, and include the verbatim statement "**Initial U.S. Approval:**" followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

YES 12. All text in the BW must be **bolded**.

Comment:

YES 13. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. Even if there is more than one warning, the term "**WARNING**" and not "**WARNINGS**" should be used. For example: "**WARNING: SERIOUS**

INFECTIONS and ACUTE HEPATIC FAILURE". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings. The BW title should be centered.

Comment:

YES 14. The BW must always have the verbatim statement "***See full prescribing information for complete boxed warning***." This statement must be placed immediately beneath the BW title, and should be centered and appear in *italics*.

Comment:

YES 15. The BW must be limited in length to 20 lines. (This includes white space but does not include the BW title and the statement "***See full prescribing information for complete boxed warning.***")

Comment:

Recent Major Changes (RMC) in Highlights

YES 16. RMC pertains to only five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the FPI.

Comment:

YES 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section's identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, "Warnings and Precautions, Acute Liver Failure (5.1) --- 8/2015."

Comment: *Noted, in xx/xxxx format currently*

NO 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

Comment: *??*

Dosage Forms and Strengths in Highlights

YES 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

Comment:

Contraindications in Highlights

YES 20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word "None."

Comment:

Selected Requirements of Prescribing Information

Adverse Reactions in Highlights

YES 21. For drug products other than vaccines, the verbatim **bolded** statement must be present: "**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer's U.S. phone number which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**"

Comment:

Patient Counseling Information Statement in Highlights

YES 22. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- **See 17 for PATIENT COUNSELING INFORMATION**

If a product **has (or will have)** FDA-approved patient labeling:

- **See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**
- **See 17 for PATIENT COUNSELING INFORMATION and Medication Guide**

Comment:

Revision Date in Highlights

YES 23. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., "**Revised: 8/2015** ").

Comment:

Contents: Table of Contents (TOC)

See Appendix for a sample tool illustrating Table of Contents format.

YES 24. The TOC should be in a two-column format.

Comment:

YES 25. The following heading must appear at the beginning of the TOC: **"FULL PRESCRIBING INFORMATION: CONTENTS."** This heading should be in all UPPER CASE letters and **bolded**.

Comment:

YES 26. The same title for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.

Comment:

YES 27. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.

Comment:

YES 28. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (for, of, to) and articles (a, an, the), or conjunctions (or, and)].

Comment:

YES 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading "**FULL PRESCRIBING INFORMATION: CONTENTS***" must be followed by an asterisk and the following statement must appear at the end of the TOC: "*Sections or subsections omitted from the full prescribing information are not listed."

Comment:

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

YES 31. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. (Section and subsection headings should be in UPPER CASE and title case, respectively.) If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use "**Labor and Delivery**")
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use "**Nursing Mothers**")
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

YES 32. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, *"[see Warnings and Precautions (5.2)]."*

Comment: *Need to follow-up with LO*

YES

33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

YES 34. The following heading "**FULL PRESCRIBING INFORMATION"** must be **bolded,** must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

YES 35. All text in the BW should be **bolded**.

Comment:

YES 36. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. (Even if there is more than one warning, the term, "**WARNING**" and not "**WARNINGS**" should be used.) For example: "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings.

Comment:

CONTRAINDICATIONS Section in the FPI

YES 37. If no Contraindications are known, this section must state "None."

Comment:

ADVERSE REACTIONS Section in the FPI

YES 38. When clinical trials adverse reactions data are included (typically in the "Clinical Trials Experience" subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

"Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice."

Comment:

YES 39. When postmarketing adverse reaction data are included (typically in the "Postmarketing Experience" subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions:

"The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure."

Comment:

PATIENT COUNSELING INFORMATION Section in the FPI

YES 40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment:

YES 41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) must not be included as a subsection under Section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Appendix: Highlights and Table of Contents Format

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.

- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)

Limitations of Use: Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

Revised: M/201Y

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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/s/

LINDA C ONAGA
06/30/2016

KAREN D WINESTOCK
06/30/2016

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 6/24/2016

TO: Division of Pulmonary, Allergy and Rheumatology Products
Office of Drug Evaluation II

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without an on-site inspection**

RE: NDA 22128/S-017

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS recently inspected the site listed below. The inspectional outcome from the inspection was classified as No Action Indicated (NAI).

Inspection Site

Facility Type	Facility Name	Facility Address
Analytical		(b) (4)

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/s/

SHILA S NKAH
06/26/2016

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 6/24/2016

TO: Division of Pulmonary, Allergy and Rheumatology Products
Office of Drug Evaluation II

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without an on-site inspection**

RE: NDA 208984

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS recently inspected the site listed below. The inspectional outcome from the inspection was classified as No Action Indicated (NAI).

Inspection Site

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	

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

/s/

SHILA S NKAH
06/26/2016