CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208351Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)
DIVISION OF ANTIVIRAL PRODUCTS (HFD-530)  
VIROLOGY REVIEW  
NDA: 208351 SDN: 001  DATE REVIEWED: 12/01/2015  
Virology Reviewer: Lisa K. Naeger, Ph.D.  

NDA#: 208351  Serial #: 000  
Reviewer’s Name(s): Lisa K. Naeger, Ph.D.  

Sponsor’s Name and Address:  
Gilead Sciences  

Initial Submission Dates:  
Correspondence Date: 07/01/15  
CDER Receipt Date: 07/01/15  
Assigned Date: 07/02/15  
Review Complete Date: 12/01/15  
PDUFA Date: March 1, 2016  

Amendments:  
SDN  CDER Stamp Date  Assigned Date  
006  09/04/2015  10/15/2015  
010  11/06/2015  11/09/2015  

Related/Supporting Documents:  
IND53971; NDA21500; IND63737; IND111007; IND67699, NDA202022, NDA202123, NDA207561  

Product Name(s):  
Proprietary:  
Non-Proprietary/USAN: rilpivirine/emtricitabine/tenofovir alafenamide  
Code Name/Number: TMC278/FTC/TAF  

<table>
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<tr>
<th>Individual Component</th>
<th>FTC</th>
<th>TAF</th>
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<tbody>
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<td>Structure</td>
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<td><img src="image" alt="TAF Structure" /></td>
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<tr>
<td>Chemical Names</td>
<td>5-fluoro-1-(2R,5S)-[2-(hydroxymethyl) -1,3-oxathiolan-5-yl]cytosine</td>
<td>L-Alanine,N-[(S)-[[1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phenoxyphosphinyl]-1-methylethyl ester (2E)-2-butenedioate</td>
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<td>Molecular Formula</td>
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<td>Drug Class</td>
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<tr>
<td>Supporting Document</td>
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Reference ID: 3854643
DIVISION OF ANTIVIRAL PRODUCTS (HFD-530)
VIROLOGY REVIEW
NDA: 208351 SDN: 001 DATE REVIEWED: 12/01/2015
Virology Reviewer: Lisa K. Naeger, Ph.D.

<table>
<thead>
<tr>
<th>Individual Component</th>
<th>Rilpivirine</th>
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<td>Structure</td>
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<td>Supporting Document</td>
<td>IND67699, NDA202022</td>
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**Dosage Form(s):**
Route(s) of Administration: Oral
Indication(s): Treatment of HIV-1 infection in ARV treatment-naive adult patients
Dispensed: Rx \(\times\) OTC

**Abbreviations:** EC_{50}, effective concentration at 50%; EFV, efavirenz; ENF, enfuvirtide; ETR, etravirine; EVG, elvitegravir; FC, fold change; HSA, human serum albumin; IC_{50}, inhibitory concentration at 50%; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NVP, nevirapine; PBL, peripheral blood lymphocytes; PI, protease inhibitor; PR, protease; RAMs, resistant-associated mutations; RPV, rilpivirine; RT, reverse transcriptase; SDM, site-directed mutants; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; TFV, tenofovir (active moiety of the diester prodrugs TAF and TDF)

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EXECUTIVE SUMMARY

This NDA is approvable with respect to virology for the treatment of HIV-1 infection in antiretroviral patients. FTC/TAF/RPV is being approved based on bioavailability studies and links the efficacy of FTC/TAF to the efficacy studies of GENVOYA™ (EVG/COBI/FTC/TAF) in NDA207561 approved on November 5, 2015. The efficacy of rilpivirine (RPV) was reviewed in NDA202022 and RPV was approved in May 2011. No significant virology issues have been identified. Labeling negotiations were ongoing at the time of finalization of this review, so labeling is not included in this review and will be included in the CDTL review. The sponsor provided an updated label in SDN010 incorporating changes made to the Microbiology section in the GENVOYA™ label.

Please refer to NDA202022 for complete virology review of rilpivirine, NDA202123 for rilpivirine/emtricitabine/tenofovir disoproxil fumarate and NDA207561 for tenofovir alafenamide.

1. RECOMMENDATIONS

1.1. RECOMMENDATION AND CONCLUSION ON APPROVABILITY:

This NDA for a fixed dose combination of emtricitabine, tenofovir alafenamide and rilpivirine fumarate is approvable from a virology perspective for the treatment of HIV-1 infection.

1.2. RECOMMENDATION ON PHASE 4 (POST-MARKETING) COMMITMENTS, AGREEMENTS, AND/OR RISK MANAGEMENT STEPS, IF APPROVABLE:

There are no phase 4 recommendations for this application.

2. ADMINISTRATIVE

2.1. Reviewer’s Signature(s)

Lisa K. Naeger
[Lisa K. Naeger, Ph.D.]
Sr. Virologist, HFD-530

2.2. Concurrence

HFD-530/Micro TL Jules O’Rear Date 12/01/2015
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LISA K NAEGER
12/02/2015

JULIAN J O REAR
12/02/2015