Clinical and Cross-Discipline Team Leader Summary Review Addendum

Date	June 17, 2019
From	Tanvir Bell, MD - Clinical Reviewer Wendy Carter, DO - CDTL
Subject	Addendum to clarify pediatric indication
NDA/BLA # and Supplement#	NDA 210251 – Supplement 5 (SDN 234)
Applicant	Gilead Sciences, Inc.
Date of Submission	December 20, 2018
PDUFA Goal Date	June 20, 2019
Proprietary Name	BIKTARVY®
Established or Proper Name	Bictegravir (BIC, B)/emtricitabine (FTC, F) /tenofovir alafenamide (TAF)
Dosage Form(s)	B/F/TAF 50/200/25 mg fixed-dose combination (FDC)
Applicant Proposed Indication(s)/Population(s)	HIV-1 infected, virologically suppressed adolescents and children
Applicant Proposed Dosing Regimen(s)	B/F/TAF 50/200/25 mg
Recommendation on Regulatory Action	*Approval*

The approval of the pediatric supplement and indication for pediatric patients weighing greater than 25 kg is most notably on the basis of PK data in HIV-1 positive virologically suppressed adolescents and children (Trial 1474). The review team evaluated the pharmacokinetic, efficacy, and safety data of Biktarvy from Trial 1474 and details can be found in the CDTL review of Supplement 5.

Biktarvy is currently indicated as a complete regimen for the treatment of HIV-1 infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy.

Efficacy for pediatric indications for the treatment of HIV is based on establishing a dosing regimen in children that results in comparable pharmacokinetic (PK) exposures in children compared to that of adults. The PK link is used to extrapolate efficacy from adults to children for all of the adult HIV treatment indications. Pediatric treatment naïve patients were not included in Trial 1474 because the ART treatment naïve population in children is small and the clear majority get HIV from perinatal transmission and are started on ART outside of clinical trials. Evaluating children who are already suppressed on a previous regimen is more feasible

for timely enrollment of pediatric trials. Because the amount of HIV treatment experience generally does not affect PK exposures, it is adequate to evaluate exposures in only one group of pediatric patients (e.g., naïve, suppressed, or treatment experienced) to make a PK link between adults and children.

The same approach with a similar virologically suppressed trial in children was used for Genvoya (Trial 0106), and Genvoya is indicated for a similar patient population (i.e. adults and pediatric population greater than 25 kg) for both naïve and suppressed HIV-1 patients.

The review team agrees with extending the indication for Biktarvy as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 25 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy from our review of pharmacokinetic, efficacy, and safety data from Trial 1474. This indication includes both populations of treatment naïve and virologically suppressed pediatric patients weighing greater than 25 kg.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

TANVIR K BELL
06/17/2019 03:51:59 PM
addendum cdtl

JEFFREY S MURRAY
06/17/2019 03:59:25 PM