

HIV Updates: BIKTARVY labeling revisions

HIV Email Updates



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FDA recently approved changes to the BIKTARVY (bictegravir, emtricitabine, and tenofovir alafenamide) tablet labeling to include the following:

- Expand the patient population for BIKTARVY® to include HIV-1 infected pediatric patients weighing at least 25 kg. This change is supported by safety and efficacy data in HIV-1 infected, virologically suppressed adolescents and children from Clinical Trial GS-US-380-1474.
- Update WARNINGS AND PRECAUTIONS, Immune Reconstitution Syndrome subsection, with autoimmune hepatitis information.
- Update DRUG INTERACTIONS, Table 3, with drug interaction information pertaining to the coadministration of BIKTARVY® with polyvalent cation (PVC) containing antacids and supplements.
- Update NONCLINICAL TOXICOLOGY, Carcinogenesis, Mutagenesis, Impairment of Fertility subsection, with the carcinogenicity data from a 2-year rate study.

A summary of the changes is as follows:

Section 1 INDICATIONS AND USAGE and **Section 2 DOSAGE AND ADMINISTRATION** were updated to include pediatric patients weighing at least 25 kg.

Section 1 INDICATIONS AND USAGE

BIKTARVY is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (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 with no history of treatment failure and no known substitutions associated with resistance to the individual components of BIKTARVY.

Section 2 DOSAGE AND ADMINISTRATION, subsection 2.2 Recommended Dosage

BIKTARVY is a three-drug fixed dose combination product containing 50 mg of bictegravir (BIC), 200 mg of emtricitabine (FTC), and 25 mg of tenofovir alafenamide (TAF). The recommended dosage of BIKTARVY is one tablet taken orally once daily with or without food in adults and pediatric patients weighing at least 25 kg

Section 5 WARNINGS AND PRECAUTIONS, subsection 5.3 Immune Reconstitution Syndrome was updated to include autoimmune hepatitis as one of the autoimmune disorders reported to occur in the setting of immune reconstitution.

Section 6 ADVERSE REACTIONS was updated to include the safety findings from the pediatric trial GS-US-380-1474.

Clinical Trials in Pediatric Subjects

The safety of BIKTARVY was evaluated in HIV-1 infected virologically-suppressed subjects between the ages of 12 to less than 18 years and weighing at least 35 kg (N=50) through Week 48 (cohort 1), and in virologically-suppressed subjects between the ages of 6 to less than 12 years and weighing at least 25 kg (N=50) through Week 24 (cohort 2) in an open label clinical trial (Trial 1474). No new adverse reactions or laboratory abnormalities were identified compared to those observed in adults. Adverse reactions were reported in 10% of pediatric subjects. The majority (85%) of adverse reactions were Grade 1. No Grade 3 or 4 adverse reactions were reported. The adverse reaction reported by more than one subject (regardless of severity) was abdominal pain (n=2). One subject (1%) had Grade 2 adverse reactions of insomnia and anxiety that led to discontinuation of BIKTARVY. The other adverse reactions that occurred in single subjects were similar to those seen in adults.

In addition, **Section 6.2 Postmarketing Experience** was added as follows:

The following events have been identified during post approval use of products containing TAF. Because these events 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.

Section 7 DRUG INTERACTIONS was updated to include revised clinical comments for medications or oral supplements containing polyvalent cations (e.g., Mg, Al, Ca, Fe).

Antacids containing Al/Mg:

BIKTARVY can be taken at least 2 hours before or 6 hours after taking antacids containing Al/Mg.

Routine administration of BIKTARVY together with, or 2 hours after, antacids containing Al/Mg is not recommended.

Supplements or antacids containing Calcium or Iron:

BIKTARVY and supplements or antacids containing calcium or iron can be taken together with food.

Routine administration of BIKTARVY under fasting conditions together with, or 2 hours after, supplements or antacids containing calcium or iron is not recommended.

The following was added to **Section 8 USE IN SPECIFIC POPULATIONS, subsection 8.4 Pediatric Use:**

The safety and effectiveness of BIKTARVY for the treatment of HIV-1 infection was established in pediatric patients with body weight greater than or equal to 25 kg.

Use of BIKTARVY in pediatric patients between the ages of 6 to less than 18 years and weighing at least 25 kg is supported by trials in adults and by an open-label trial in virologically-suppressed pediatric subjects aged 12 to less than 18 years and weighing at least 35 kg receiving BIKTARVY through Week 48 (cohort 1 of Trial 1474, N=50) and in virologically-suppressed pediatric subjects aged 6 to less than 12 years and weighing at least 25 kg receiving BIKTARVY through Week 24 (cohort 2 of Trial 1474, N=50). The safety and efficacy of BIKTARVY in these pediatric subjects was similar to that in adults, and there was no clinically significant change in exposure for the components of BIKTARVY.

Safety and effectiveness of BIKTARVY in pediatric patients weighing less than 25 kg have not been established.

Section 12 CLINICAL PHARMACOLOGY subsection 12.3 Pharmacokinetics was updated to include the pharmacokinetic data from Trial GS-US-380-1474. Please refer to product labeling for more details.

Pediatric Patients

Mean BIC Ctrough was lower in 50 pediatric patients aged 12 to less than 18 years and weighing at least 35 kg who received BIKTARVY in Trial 1474 relative to adults following administration of BIKTARVY, but was not considered clinically significant based on exposure-response relationships; exposures of FTC and TAF in these pediatric patients were similar to those in adults.

Mean BIC Cmax, and exposures of FTC and TAF (AUCtau and Cmax) achieved in 50 pediatric patients between the ages of 6 to less than 12 years and weighing at least 25 kg who received BIKTARVY in Trial 1474 were higher than exposures in adults; however, the increase was not considered clinically significant as the safety profiles were similar in adult and pediatric patients.

Section 12.4 Microbiology was updated as follows:

In Virologically Suppressed Pediatric Subjects: In Trial 1474, two of 50 subjects in cohort 1, were evaluated for the development of resistance through Week 48; no amino acid substitutions known to be associated with resistance to BIC, FTC, or TFV were detected. No subjects in cohort 2 met criteria for resistance analyses.

The following text was added to **Section 13 NONCLINICAL TOXICOLOGY, subsection, 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility:**

- BIC was not carcinogenic in a 2-year rat study at doses up to 300 mg/kg/day, which resulted in exposures of approximately 31 times the exposure in humans at the recommended dose of BIKTARVY

Section 14 Clinical Studies was updated to include the efficacy results from Trial GS-US-380-1474.

14.4 Clinical Trial Results in HIV-1 Infected Pediatric Subjects Between the Ages of 6 to Less than 18 Years

In Trial 1474, an open-label, single arm trial the efficacy, safety, and pharmacokinetics of BIKTARVY in HIV-1 infected pediatric subjects were evaluated in virologically-suppressed adolescents between the ages of 12 to less than 18 years weighing at least 35 kg (N=50) and in virologically-suppressed children between the ages of 6 to less than 12 years weighing at least 25 kg (N=50).

Cohort 1: Virologically-suppressed adolescents (12 to less than 18 years; at least 35 kg)

Subjects in cohort 1 treated with BIKTARVY once daily had a mean age of 14 years (range: 12 to 17) and a mean baseline weight of 51.7 kg (range: 35 to 123), 64% were female, 27% were Asian and 65% were black. At baseline, median CD4+ cell count was 750 cells per mm³ (range: 337 to 1207), and median CD4+% was 33% (range: 19% to 45%).

After switching to BIKTARVY, 98% (49/50) of subjects in cohort 1 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 48. The mean change from baseline in CD4+ cell count at Week 48 was -22 cells per mm³.

Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

Subjects in cohort 2 treated with BIKTARVY once daily had a mean age of 10 years (range: 6 to 11) and a mean baseline weight of 31.9 kg (range: 25 to 69), 54% were female, 22% were Asian and 72% were black. At baseline, median CD4+ cell count was 898 cells per mm³ (range 390 to 1991) and median CD4+% was 37% (range: 19% to 53%).

After switching to BIKTARVY, 100% (50/50) of subjects in cohort 2 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 24. The mean change from baseline in CD4+ cell count at Week 24 was -24 cells per mm³.

The updated label will soon be available at Drugs@FDA or DailyMed

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