Bixlenvo™ (bictegravir/lenacapavir) Use During Lactation

This document is in response to your request for information regarding Bixlenvo™ (bictegravir/lenacapavir [BIC/LEN]) or its components for the treatment of HIV-1 in individuals who are breastfeeding.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/BIXLENVO/BIXLENVO_pi.

Summary

Product Labeling[1]

Data from the published literature reports on the presence of BIC in human milk. There are no data on the effects of BIC on the breastfed child. There is no data on the effects of BIC on milk production.

LEN is present in human milk. LEN was detected at very low levels in infants who were breastfed by individuals who became pregnant while receiving LEN via injection. No adverse effects of LEN in breastfed infants have been observed. It is not known if LEN affects milk production.

Potential risks of breastfeeding include: (1) HIV-1 transmission to HIV-1–negative infants; (2) developing viral resistance in HIV-1–positive infants; and (3) adverse reactions in a breastfed infant similar to those seen in adults.

The median LEN concentration in human breast milk to maternal plasma ratio in participants (n=8) who received LEN via injection was 0.63 (range: 0.29 to 1.90). The median infant-to-mother plasma ratio for LEN in infants (n=10) who were breastfed by individuals receiving LEN via injection from 0 to <13 weeks after delivery was 0.06 (range: 0.01 to 0.20). Data are not available in breastfeeding individuals receiving LEN orally.

Clinical Data on the Use of BIC/LEN Components During Lactation

Breastfeeding participants were excluded from the phase 2/3 ARTISTRY-1 and phase 3 ARTISTRY-2 studies that assessed the efficacy and safety of BIC + LEN in VS PWH.[2-5]

In a PK study evaluating breast milk and plasma concentrations of BIC in women without HIV after a single dose of BIC/FTC/TAF, exposure to BIC through breast milk was very low, with a relative infant dose below 1%.[6]

In a nested PK substudy of participants without HIV-1 in PURPOSE 1 who were randomly assigned to the SUBQ LEN group and became pregnant during the study, LEN concentrations remained generally consistent throughout pregnancy and postpartum, with no evident trimester-related changes. Subsequent population PK analyses demonstrated no statistically significant differences in LEN exposure when comparing pregnancy trimesters,

postpartum status, and non-pregnant individuals. Further PK analyses showed LEN exposures were similar between pregnant and non-pregnant participants. LEN was found in breast milk, but LEN concentrations were very low in breastfed infants.[7]

Clinical Data on the Use of BIC/LEN Components During Lactation

BIC/LEN

ARTISTRY-1 (GS-US-621-6289) is an ongoing, randomized, multicenter, open-label, phase 2/3 study designed to evaluate the efficacy and safety of switching to oral BIC/LEN (75 mg/50 mg) vs continuing a complex ART regimen in VS PWH.[2]

ARTISTRY-2 (GS-US-621-6290) is an ongoing, randomized, multicenter, double-blind, active-controlled phase 3 study designed to evaluate the efficacy and safety of switching from BIC/FTC/TAF to oral BIC/LEN (75 mg/50 mg) vs continuing BIC/FTC/TAF in VS PWH.[3]

Breastfeeding participants were excluded from both studies.[4,5]

BIC[6]

Twelve healthy lactating women without HIV received a single dose of BIC/FTC/TAF and samples of blood and breast milk were collected at regular intervals up to 24 hours post ingestion. Eligible participants had a median age of 33 (32–33.8) years, median BMI of 24.8 (23.9–28.4) kg/m², and were a median of 10 (5.3–15.3) months postpartum, with infants weighing a median of 8.8 (7.2–10) kg at the time of evaluation. Plasma and breast milk drug concentrations were measured via a validated LC-MS/MS assay and PK parameters were calculated using non-compartmental analysis. A total of 132 plasma and 72 breast milk samples were collected. All concentrations fell within the quantifiable range.

The geometric mean (CV%) AUC_{last} was 52.17 (22.6) mg*h/L in plasma and 0.44 (32.0) mg*h/L in breast milk, resulting in a geometric mean (CV%) breast milk to maternal plasma ratio of 0.009 (26.6). Additional BIC PK parameters for plasma and breast milk are listed in Table 1.

Table 1. BIC PK concentrations in plasma and breast milk

Pharmacokinetic parameters	Plasma [GM CV%]	Breast milk [GM CV%]
AUC_{inf} (mg*h/L)	79.03 (28.8)	0.75 (40.5)
AUC_{last} (mg*h/L)	52.17 (22.6)	0.44 (32.0)
C_{max} (mg/L)	4.634 (17.4)	0.030 (25.8)
T_{max} (hours)	1.19 (45.2)	3.13 (52.2)
$T_{1/2}$ (hours)	15.5 (18.5)	17.2 (28.5)

The authors reported exposure to BIC through breast milk was very low, with a relative infant dose below 1%. No SAEs were reported. All reported AEs were grade 1-2, including one possibly drug-related lab change in bilirubin. The study limitations were only single-dose of BIC/FTC/TAF was evaluated and transmission of HIV or clinical outcomes were not assessed.

LEN

PURPOSE 1 (NCT04994509) is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TAF for HIV-1 PrEP in cisgender women and adolescent girls across South Africa and Uganda. Additionally, a third group was assigned once-daily oral FTC/TDF, which served as the active control. Participants who discontinued blinded study drug were given the option to take open-label FTC/TDF. Randomized participants had body weight ≥35 kg and eGFR ≥60 mL/min.[8]

A nested PK substudy of participants who were randomly assigned to the LEN group and became pregnant during the study was conducted to assess systemic LEN concentrations during pregnancy and postpartum, as well as LEN concentrations in breast milk and infants. Maternal plasma PK samples were collected in regular intervals throughout the first, second, and third trimesters, and maternal plasma, infant plasma, and breast milk samples were obtained at approximately 3 and 6 months postpartum.[7]

Overall, 601 participants were included in the population PK analysis, including 296 participants who became pregnant while receiving LEN and had at least one quantifiable PK sample collected during pregnancy. Pregnant participants received SUBQ LEN injections in the thigh or abdomen.[7] At Weeks 26, 52, and 78, C_{trough} data were available from 107 first-trimester, 99 second-trimester, 59 third-trimester, and 65 postpartum visits.[9]

No observable trimester-related trends in LEN were identified across pregnancy trimesters or during the postpartum period.[7] Model-derived LEN C_{max} and C_{trough} concentrations were comparable across participants between pregnancy trimesters, postpartum, and non-pregnant individuals.[9] Population PK analyses further demonstrated that gestational age, pregnancy trimester, and postpartum status were not statistically significant covariates of LEN exposure. LEN PK were also similar when LEN was injected in the thigh or the abdomen.[7]

LEN was found in breast milk, but LEN concentrations were very low in breastfed infants. In 102 matched pairs, the median (IQR) breast milk-to-maternal plasma ratio was 0.52 (0.38–0.77). In 98 matched pairs, the median (IQR) breastfed-infant-to-maternal plasma ratio was 0.02 (0.01–0.05). No adverse effects were identified among breastfed infants exposed to LEN.[7]

References

1. Enclosed, Gilead Sciences Inc. TRADENAME™ (bictegravir and lenacapavir) tablets, for oral use. U.S. Prescribing Information. Foster City, CA. 2026.
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Abbreviations

%CV=percent coefficient of variation
AE=adverse event
ART=antiretroviral therapy
AUC=area under the concentration-time curve
BIC=bictegravir
C_{max}=peak concentration
C_{trough}=trough plasma concentration
eGFR=estimated glomerular filtration rate
FTC=emtricitabine
GM=geometric mean
IQR=interquartile range
LC-MS/MS=liquid chromatography tandem mass spectrometry
LEN=lenacapavir
PK=pharmacokinetic
PrEP=pre-exposure prophylaxis
PWH=people with HIV
SAE=serious adverse event
SUBQ=subcutaneous
$t_{1/2}$=elimination half-life
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
VS=virologically suppressed

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Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the BIXLENVO US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/BIXLENVO/BIXLENVO_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

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Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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