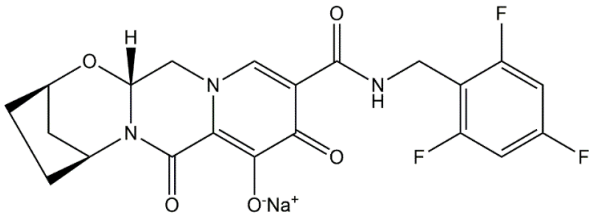
Bictegravir PK Fact Sheet

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Details

Generic Name	Bictegravir
Trade Name	Biktarvy® (50 mg bictegravir, with emtricitabine, tenofovir alafenamide fumarate) Bixlenvo® (75 mg bictegravir, with lenacapavir)
Class	Integrase Inhibitor
Molecular Weight	471.4
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	Pharmacokinetics are dose proportional over the dose range of 25 to 100 mg
Steady state	10 days[1]
Plasma half life	*As Biktarvy:* 17.3 h *As Bixlenvo:* 19.3 to 21 h
Cmax	*As Biktarvy:* 6.15 µg/mL (22.9%), mean (%CV), [at steady state in adults with HIV] *As Bixlenvo:* 8600 ng/ml (29.0%), mean (%CV), [steady state exposures from population PK analyses in adults with HIV]
Ctrough	*As Biktarvy:* 2.61 µg/mL (35.2%), mean (%CV), [at steady state in adults with HIV] *As Bixlenvo:* 4660 ng/ml (39.8%), mean (%CV), [steady state exposures from population PK analyses in adults with HIV]
AUC	*As Biktarvy:* 102 µg.h/mL (26.9%), mean (%CV), [at steady state in adults with HIV] *As Bixlenvo:* 154000 ng.h/ml (33.3%), mean (%CV), [steady state exposures from population PK analyses in adults with HIV]
Bioavailability	Not determined
Absorption	*As Biktarvy:* Relative to fasting conditions, administration with a high fat meal (~800 kcal, 50% fat) increased bictegravir AUC and Cmax by 24% and 13%. A similar effect was observed with a moderate fat meal (~600 kcal, 27% fat). Biktarvy can be taken with or without food. *As Bixlenvo:* Relative to fasting conditions, administration with a high fat meal (~800 kcal, 50% fat) increased bictegravir AUC and Cmax by 12% and 16%. A similar effect was observed with a moderate fat meal (~600 kcal, 27% fat). Bixlenvo can be taken with or without food.
Protein Binding	>99%
Volume of Distribution	15.56 L [1]
CSF:Plasma ratio	Not determined
Semen:Plasma ratio	Not determined
Renal Clearance	35% (primarily of the glucuronide and other minor oxidative metabolites and their phase II conjugates). Renal excretion of intact bictegravir is a minor pathway (~1% of dose).

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Dosing in Renal and Hepatic Impairment

Renal Impairment

No clinically relevant differences in bictegravir pharmacokinetics were observed between healthy subjects and subjects with severe renal impairment (estimated CrCl 15-29 mL/min). In a study of virologically-suppressed participants with ESRD (estimated creatinine clearance less than 15 mL/min, by Cockcroft-Gault method) receiving chronic haemodialysis who were receiving a Biktarvy, median bictegravir Ctrough values in participants with ESRD (n=7) were 846 ng/mL (range 288-1810) compared to 2540 ng/mL (range 757-6499) in participants with normal renal function(n=584). Despite significantly lower bictegravir Ctrough values in the virologically-suppressed ESRD population, virologic suppression was maintained.

As Biktarvy: No dose adjustment of Biktarvy is required in patients with estimated CrCl ≥30 mL/min. Biktarvy is not recommended in patients with estimated CrCl below 30 mL/min.

As Bixlenvo: No dosage adjustment of Bixlenvo is recommended in patients with mild, moderate or severe renal impairment (estimated CrCl ≥15 mL/minute). Bixlenvo has not been studied in patients with end-stage renal disease (ESRD; CrCl <15 mL/minute)

Hepatic Impairment

Clinically relevant changes in the pharmacokinetics of bictegravir were not observed in subjects with moderate (Child-Pugh Class B) hepatic impairment.

As Biktarvy: No dose adjustment of Biktarvy is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Biktarvy has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and is not recommended for use in these patients.

As Bixlenvo: No dosage adjustment of Bixlenvo is recommended in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Bixlenvo has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

Metabolism and Distribution

Metabolised by	Primarily by CYP3A and UGT1A1.
Inhibitor of	OCT2 and MATE1. At clinically relevant concentrations, bictegravir is not an inhibitor of CYP (including CYP3A) or UGT1A1 enzymes, the hepatic transporters OATP1B1, OATP1B3, OCT1, BSEP, or the renal transporters OAT1 and OAT3.
Inducer of	Does not induce CYP (including CYP3A) enzymes.
Transported by	P-gp, BCRP.

References

Unless otherwise stated (see below), information is from:

Biktarvy® Summary of Product Characteristics, Gilead Sciences Ltd.
Biktarvy® Prescribing Information, Gilead Sciences Inc.
Bixlenvo® Prescribing Information, Gilead Sciences Inc.

1. Antiviral activity, safety, and pharmacokinetics of bictegravir as 10-day monotherapy in HIV-1–infected adults. Gallant JE, Thompson M, DeJesus E, et al. *J Acquir Immune Defic Syndr*, 2017, **75(1):** 61-66.

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