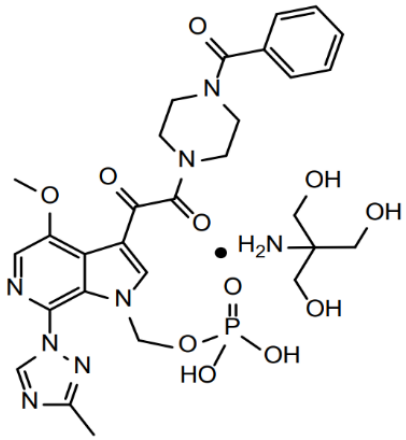
Fostemsavir PK Fact Sheet

Details

Generic Name	Fostemsavir
Trade Name	Rukobia®
Class	Entry Inhibitor - HIV-1 gp120-directed attachment inhibitor
Molecular Weight	704.3 (583.5 as free acid)
Structure	

Summary of Key Pharmacokinetic Parameters

Fostemsavir is a prodrug of temsavir, its active moiety. Fostemsavir was generally not detectable in plasma following oral administration, however, temsavir was readily absorbed. Values for temsavir are given below.

Linearity/non-linearity	Following oral administration of 600-1800 mg fostemsavir, increases in plasma temsavir exposure appeared dose proportional or slightly greater than dose proportional.
Steady state	Following twice daily oral administration, fostemsavir was rapidly converted to temsavir reaching steady state after 2-3 days. [1]
Plasma half life	11 h
Cmax	1770 ng/ml
Ctau	478 ng/ml
AUC	12900 ng.h/ml
Bioavailability	26.9%
Absorption	Relative to fasting, temsavir AUC increased by 10% with a standard meal and by 81% with a high fat meal.
Protein Binding	88.4
Volume of Distribution	29.5 L
CSF:Plasma ratio	Not evaluated
Semen:Plasma ratio	Not evaluated
Renal Clearance	51%; <2% as unchanged drug

Dosing in Renal and Hepatic Impairment

Renal Impairment	No dosage adjustment is required for patients with renal impairment or those on haemodialysis. No clinically relevant differences in total and unbound temsavir pharmacokinetics were observed in patients with mild to severe renal impairment. No clinically relevant differences in temsavir pharmacokinetics were observed in patients with end-stage renal disease (ESRD) on haemodialysis compared with the same patients with ESRD off haemodialysis. Temsavir was not readily cleared by haemodialysis with approximately 12.3% of the administered dose removed during the 4-hour haemodialysis session
Hepatic Impairment	No dosage adjustment is required in patients with hepatic impairment. No clinically relevant differences in total and unbound temsavir pharmacokinetics were observed in patients with mild to severe hepatic impairment (Child-Pugh Score A, B, or C)

Metabolism and Distribution

Metabolised by	Esterases (36.1% of oral dose); CYP3A4 (21.2% of oral dose); UGT (<1% of oral dose)
Inducer of	Based on in vitro and clinical drug interaction data, significant interactions are not expected with substrates of CYPs, UGTs, P-gp, MRP2, BSEP, NTCP, OAT1, OAT3, OCT1, and OCT2.
Inhibitor of	OATP1B1, OATP1B3, BCRP Based on in vitro data, temsavir and its two metabolites (BMS-646915 and BMS-930644) inhibited MATE1/2K but this is unlikely to be of clinical significance.
Transported by	P-gp, BCRP

References

Unless otherwise stated (see below), information is from:
Rukobia® Summary of Product Characteristics, ViiV Healthcare.
Rukobia® US Prescribing Information, ViiV Healthcare.

1. Nettles R, Chien C, Elefant E, et al. Single and multiple dose pharmacokinetics and safety in non-HIV-infected healthy subjects dosed withBMS-663068, an oral HIV attachment inhibitor. 12th International Workshop on Clinical Pharmacology of HIV Therapy, Miami, April 2011, abstract O_04.