### Details

**Generic Name**  
Fostemsavir

**Trade Name**  
Rukobia®

**Class**  
Enter Inhibitor - HIV-1 gp120-directed attachment inhibitor

**Molecular Weight**  
704.3 (583.5 as free acid)

**Structure**  
![Fostemsavir Structure](image)

### 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 temsivir pharmacokinetics were observed in patients with mild to severe renal impairment. No clinically relevant differences in temsivir pharmacokinetics were observed in patients with end-stage renal disease (ESRD) on haemodialysis compared with the same patients with ESRD off haemodialysis. Temsivir 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 temsivir 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, temsivir 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: