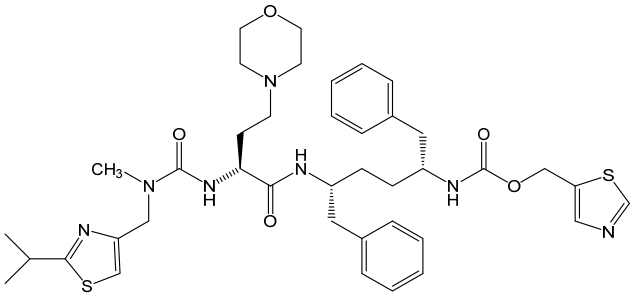
Cobicistat PK Fact Sheet

Details

Generic Name	Cobicistat
Trade Name	Tybost®
Class	Pharmacokinetic enhancer/booster (CYP3A inhibitor)
Molecular Weight	776.0
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	Cobicistat exposures are non-linear and greater than dose-proportional over 50-400 mg, consistent with a mechanism-based CYP3A inhibitor.
Steady state	Not determined
Plasma half life	~3-4 h
Cmax	1.2 ± 0.3 µg/ml 1.1 ± 0.4 µg/ml (in combination with elvitegravir, emtricitabine, tenofovir-DF)
Cmin	0.07 ± 0.07 µg/ml 0.05 ± 0.13 µg/ml (in combination with elvitegravir, emtricitabine, tenofovir-DF)
AUC	10.9 ± 3.8 µg.h/ml 8.3 ± 3.8 µg.h/ml (in combination with elvitegravir, emtricitabine, tenofovir-DF)
Bioavailability	Not determined
Absorption	A food effect trial was not conducted for cobicistat alone. Relative to fasting conditions, the administration of a single dose of cobicistat and elvitegravir, emtricitabine and tenofovir-DF with a light meal (~373 kcal, 20% fat) or a high fat meal (~ 800 kcal, 50% fat)had no clinically significant effect on cobicistat systemic exposure. It is recommended that cobicistat be administered with food.
Protein Binding	97-98%
Volume of Distribution	Not determined
CSF:Plasma ratio	Not determined
Semen:Plasma ratio	Not determined
Renal Clearance	Minor route (~8%)
Renal Impairment	No dose adjustment is required for patients with renal impairment, including those with severe renal impairment. Cobicistat has not been studied in patients receiving dialysis, and, therefore, no recommendation can be made for these patients. Cobicistat has been shown to decrease estimated creatinine clearance due to inhibition of tubular secretion of creatinine and should not be initiated in patients with creatinine clearance <70 ml/min if any co-administered agent (e.g. emtricitabine, lamivudine, tenofovir disoproxil fumarate, or adefovir) requires dose adjustment based on creatinine clearance.
Hepatic Impairment	No dose adjustment is required in patients with mild (Child-Pugh Class A) or moderate hepatic impairment (Child-Pugh Class B). Cobicistat has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), therefore, its use is not recommended in these patients

Metabolism and Distribution

Metabolised by	CYP3A, CYP2D6 (minor)
Inducer of	Does NOT induce CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19 or UGT1A1 (*cf*. ritonavir) Not expected to induce CYP3A4, CYP1A2, CYP2B6, P-gp, MDR1 Effect on CYP2C9, CYP2C19 and UGT1A1 is unknown but is expected to be low.
Inhibitor of	CYP3A, CYP2D6, P-gp, BCRP, MATE1, OATP1B1, OATP1B3 Not expected to inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9 or CYP2C19
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References

Unless otherwise stated (see below), information is from:
Tybost® Summary of Product Characteristics, Gilead Sciences Ltd,.
Tybost® US Prescribing Information, Gilead Sciences Inc.
Stribild® Summary of Product Characteristics, Gilead Sciences Ltd.
Stribild® US Prescribing Information, Gilead Sciences Inc.

1. Lepist EI, Zhang X, Hao J, *et al.* Contribution of the organic anion transporter OAT2 to the renal active tubular secretion of creatinine and mechanism for serum creatinine elevations caused by cobicistat. *Kidney Int.* 2014; 86(2): 350-7.