### Cabotegravir (IM) PK Fact Sheet

**Details**

**Generic Name**  
Cabotegravir  

**Trade Name**  
Vocabria®, Cabenuva® (co-packaged with rilpivirine)  

**Class**  
Integrase Inhibitor  

**Molecular Weight**  
405.35  

**Structure**

![Cabotegravir Structure](image)

### Summary of Key Pharmacokinetic Parameters

**Linearity/non-linearity**  
Plasma cabotegravir exposure increases in proportion or slightly less than in proportion to dose following single and repeat IM injection of doses ranging from 100 to 800 mg.

**Steady state**  
Following a single intramuscular dose, plasma cabotegravir concentrations are detectable on the first day and gradually rise to reach maximum plasma concentration with a median Tmax of 7 days. Pharmacokinetic steady-state is achieved by 44 weeks.

**Plasma half life**  
~5.6 to 11.5 weeks  
Residual concentrations of cabotegravir may remain in the systemic circulation of patients for prolonged periods (up to 12 months or longer).

**Cmax**  
4.2 µg/ml (400 mg IM monthly)  
4.0 µg/ml (600 mg IM every 2 months)

**Ctau**  
2.8 µg/ml (week 48 data for a 1-month interval following 400 mg IM monthly)  
1.6 µg/ml (week 48 data for a 2-month interval following 600 mg IM every 2 months)

**AUC**  
2415 µg.h/ml (400 mg IM monthly)  
3764 µg.h/ml (600 mg IM every 2 months)

**Bioavailability**  
The absolute bioavailability of cabotegravir has not been established.

**Absorption**  
Cabotegravir injection exhibits absorption rate-limited kinetics (i.e., flip-flop pharmacokinetics) resulting from slow absorption from the gluteal muscle into the systemic circulation resulting in sustained plasma concentrations.

**Protein Binding**  
>99.8

**Volume of Distribution**  
12.3L (following oral administration)

**CSF:Plasma ratio**  
0.003

**Semen:Plasma ratio**  
Not evaluated in humans

**Renal Clearance**  
27%; 0% as unchanged drug (following oral administration)
### Dosing in Renal and Hepatic Impairment

**Renal Impairment**  
No clinically important pharmacokinetic differences between subjects with severe renal impairment (CrCL <30 mL/min and not on dialysis) and matching healthy subjects were observed. No dosage adjustment is necessary for patients with mild to severe renal impairment (not on dialysis). Cabotegravir has not been studied in patients with end-stage renal disease on renal replacement therapy. As cabotegravir is greater than 99% protein bound, dialysis is not expected to alter exposures of cabotegravir. If administered in a patient on renal replacement therapy, cabotegravir should be used with caution.

**Hepatic Impairment**  
No clinically important pharmacokinetic differences between subjects with moderate hepatic impairment and matching healthy subjects were observed. No dosage adjustment is necessary for patients with mild to moderate hepatic impairment (Child-Pugh Score A or B). The effect of severe hepatic impairment (Child-Pugh Score C) on the pharmacokinetics of cabotegravir has not been studied. If administered in a patient with severe hepatic impairment, cabotegravir should be used with caution.

### Metabolism and Distribution

**Metabolised by**  
Primarily UGT1A1, with a minor contribution from UGT1A9.

Simulations using PBPK modeling show that no clinically significant interaction is expected during coadministration of cabotegravir with drugs that inhibit UGT1A1.

Medicinal products which are strong inducers of UGT1A1 or UGT1A9 are expected to decrease cabotegravir plasma concentrations leading to lack of efficacy.

**Inducer of**  
In vitro, cabotegravir did not induce CYP1A2, CYP2B6, or CYP3A4.

**Inhibitor of**  
In vivo, oral cabotegravir did not have an effect on midazolam, a CYP3A4 probe.

In vitro, cabotegravir inhibited renal OAT1 (IC50=0.81 µM) and OAT3 (IC50=0.41 µM). Based on physiologically based pharmacokinetic (PBPK) modeling, cabotegravir may increase the AUC of OAT1/3 substrates up to approximately 80%. Therefore, caution is advised when co-dosing with OAT1/3 substrates with a narrow therapeutic index.

Cabotegravir is not a clinically relevant inhibitor of the following enzymes and transporters: CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, UGT1A1, UGT1A3, UGT1A4, UGT1A6, UGT1A9, UGT2B4, UGT2B7, UGT2B15, and UGT2B17, P-gp, BCRP, BSEP, OCT1, OCT2, OATP1B1, OATP1B3, MATE 1, MATE 2-K, MRP2 or MRP4.

**Transported by**  
Cabotegravir is a substrate of P-gp and BCRP, however, because of its high permeability, no alteration in absorption is expected when coadministered with either P-gp or BCRP inhibitors.

In vitro, cabotegravir was not a substrate of OATP1B1, OATP1B3 or OCT1.

### References

Unless otherwise stated (see below), information is from:  
Cabenuva® US Prescribing Information, Viiv Healthcare.