

# Rilpivirine (IM) PK Fact Sheet

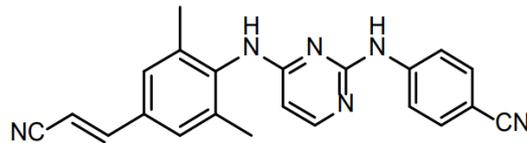
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## Details

<b>Generic Name</b>	Rilpivirine
<b>Trade Name</b>	Rekambys®; Cabenuva® (co-packaged with cabotegravir)
<b>Class</b>	Non-Nucleoside Reverse Transcriptase Inhibitor
<b>Molecular Weight</b>	366.42
<b>Structure</b>	



## Summary of Key Pharmacokinetic Parameters

<b>Linearity/non-linearity</b>	Plasma rilpivirine exposure increases in proportion or slightly less than in proportion to dose following single and repeat IM injections of doses ranging from 300 to 1200 mg.
<b>Steady state</b>	Following a single intramuscular dose, rilpivirine plasma concentrations are detectable the first day and gradually rise to reach maximum plasma concentrations after a median of 3-4 days. After 1 year of monthly or every 2 months injections, approximately 80% of the rilpivirine pharmacokinetic steady-state exposure is reached.
<b>Plasma half life</b>	~13 to 28 weeks Residual concentrations of rilpivirine may remain in the systemic circulation of patients for prolonged periods (up to 4 years in some patients) and should be considered upon discontinuation of rilpivirine injections.
<b>C<sub>max</sub></b>	120 ng/ml (600 mg IM monthly) 133 ng/ml (900 mg IM every 2 months)
<b>C<sub>tau</sub></b>	84.9 ng/ml (week 48 data for a 1-month interval following 600 mg IM monthly injections) 65.6 ng/ml (week 48 data for a 2-month interval following 900 mg IM every 2 months)
<b>AUC</b>	67703 ng.h/ml (600 mg IM monthly) 127031 ng.h/ml (900 mg IM every 2 months)
<b>Bioavailability</b>	Absolute bioavailability not determined due to lack of an IV formulation <sup>[1]</sup>
<b>Absorption</b>	Rilpivirine prolonged-release 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 rilpivirine plasma concentrations.
<b>Protein Binding</b>	99.7%
<b>Volume of Distribution</b>	~132 L
<b>CSF:Plasma ratio</b>	0.01
<b>Semen:Plasma ratio</b>	Not evaluated in humans
<b>Renal Clearance</b>	6%; <1% as unchanged drug (following oral administration)

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## Dosing in Renal and Hepatic Impairment

<i>Renal Impairment</i>	Renal elimination of rilpivirine is negligible. Based on population pharmacokinetic analyses of oral rilpivirine, no dose adjustment is needed for patients with mild or moderate renal impairment. In patients with severe renal impairment or end-stage renal disease, intramuscular rilpivirine should be used with caution and with increased monitoring for adverse effects. In patients with end-stage renal disease not on dialysis, effects on the pharmacokinetics of cabotegravir or rilpivirine are unknown. In patients with severe renal impairment or end-stage renal disease, the combination of intramuscular rilpivirine with a strong CYP3A inhibitor should only be used if the benefit outweighs the risk. As rilpivirine is highly bound to plasma proteins, it is unlikely that it will be significantly removed by haemodialysis or peritoneal dialysis
<i>Hepatic Impairment</i>	In a study comparing 8 subjects with mild hepatic impairment (Child-Pugh score A) to 8 matched controls, and 8 subjects with moderate hepatic impairment (Child-Pugh score B) to 8 matched controls, the multiple dose exposure of oral rilpivirine was 47% higher in subjects with mild hepatic impairment and 5% higher in subjects with moderate hepatic impairment. No dose adjustment is required in patients with mild or moderate hepatic impairment, but caution is advised in patients with moderate hepatic impairment. Rilpivirine has not been studied in subjects with severe hepatic impairment (Child-Pugh score C). Therefore, intramuscular rilpivirine is not recommended in patients with severe hepatic impairment

## Metabolism and Distribution

<i>Metabolised by</i>	Primarily CYP 3A. Potential contribution from CYP2C19 <sup>[1]</sup> .
<i>Inducer of</i>	At the recommended dose of 25 mg once daily, rilpivirine is not likely to have a clinically relevant effect on the exposure of medicinal products metabolised by CYP enzymes.
<i>Inhibitor of</i>	At the recommended dose of 25 mg once daily, rilpivirine is not likely to have a clinically relevant effect on the exposure of medicinal products metabolised by CYP enzymes.  Rilpivirine inhibits P-gp in vitro with an IC <sub>50</sub> of 9.2 µM. In a clinical study, oral rilpivirine (25 mg once daily) did not significantly affect the pharmacokinetics of digoxin.  Rilpivirine is an in vitro inhibitor of the transporter MATE-2K with an IC <sub>50</sub> of <2.7 nM. The clinical implications of this finding are currently unknown.
<i>Transported by</i>	Not significantly transported by P-gp <sup>[1]</sup> .

## References

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

Rekambys® [Summary of Product Characteristics](#), Janssen-Cilag Ltd.

Cabenuva® [US Prescribing Information](#), ViiV Healthcare.

1. FDA, Rilpivirine Clinical Pharmacology and Biopharmaceutics Review (NDA 202-022)  
[http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2011/202022Orig1s000TOC.cfm](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/202022Orig1s000TOC.cfm)