Ritonavir PK Fact Sheet

**Details**

**Generic Name**  
Ritonavir

**Trade Name**  
Norvir®

**Class**  
Protease Inhibitor

**Molecular Weight**  
720.95

**Structure**

![Structure of Ritonavir](image)

**Summary of Key Pharmacokinetic Parameters**

**Steady state**  
Upon multiple dosing, ritonavir accumulation is slightly less than predicted from a single dose due to a time and dose-related increase in apparent clearance (Cl/F). Trough concentrations of ritonavir decrease over time, possibly due to enzyme induction, but appeared to stabilise by the end of 2 weeks.

**Plasma half life**  
3-5 h (600 mg twice daily)  
~5 h (100 mg twice daily or once daily)

**Cmax**  
11.2 ± 3.6 µg/ml (600 mg twice daily)  
0.84 ± 0.39 µg/ml (100 mg once daily)  
0.89 µg/ml (100 mg twice daily)

**Cmin**  
3.7 ± 2.6 µg/ml (600 mg twice daily)  
0.08 ± 0.04 µg/ml (100 mg once daily)  
0.22 µg/ml (100 mg twice daily)

**AUC**  
77.5 ± 31.5 µg/ml.hr (600 mg twice daily)  
6.6 ± 2.4 µg/ml.hr (100 mg once daily)  
6.2 µg/ml.hr (100 mg twice daily)

**Bioavailability**  
Not determined

**Absorption**  
Food slightly decreases the bioavailability of the ritonavir tablet. Administration of ritonavir (100 mg single dose) with a moderate fat meal (857 kcal, 31% calories from fat) or a high fat meal (907 kcal, 52% calories from fat) was associated with a mean decrease of 20-23% in ritonavir AUC and Cmax.

**Protein Binding**  
98-99%

**Volume of Distribution**  
20-40 L (600 mg single dose)

**CSF:Plasma ratio**  
0.0-0.52 [1]

**Semen:Plasma ratio**  
<0.04 [2]

**Renal Clearance**  
3.5% as unchanged drug
Renal Impairment
Renal clearance of ritonavir is negligible; a decrease in total body clearance is not expected in renal impairment. There are currently no data specific to this patient population.

Hepatic Impairment
Pharmacokinetic data indicate that no dose adjustment is necessary in mild to moderate hepatic impairment. Ritonavir should not be given to patients with severe hepatic impairment. Ritonavir should not be given as a pharmacokinetic enhancer to patients with decompensated liver disease. In the absence of pharmacokinetic studies in patients with stable severe hepatic impairment (Child Pugh Grade C) without decompensation, caution should be exercised as increased levels of the co-administered PI may occur.

Metabolism and Distribution

<table>
<thead>
<tr>
<th>Metabolised by</th>
<th>CYP3A, CYP2D6</th>
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</thead>
<tbody>
<tr>
<td>Inducer of</td>
<td>CYP1A2, CYP2C8, CYP2C9 and CYP2C19, MRP1 expression[^3]</td>
</tr>
<tr>
<td>Inhibitor of</td>
<td>CYP3A, CYP2D6, P-glycoprotein[^4], MRP1[^5], OATP-C[^6], BCRP[^7]</td>
</tr>
<tr>
<td>Transported by</td>
<td>P-glycoprotein[^4], MRP1[^5]</td>
</tr>
</tbody>
</table>

References

Unless otherwise stated (see below), information is from:
Norvir® Tablets Summary of Product Characteristics, AbbVie Ltd.
Norvir® Tablets US Prescribing Information, AbbVie Inc.


