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Summary of Key Pharmacokinetic Parameters

Sorafenib PK Fact Sheet

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Details

Generic Name Trade Name	Sorafenib Nexavar®			
Class	HCC protein kinase inhibitor			
Molecular Weight	637			
Structure	$\begin{array}{c} F \\ C \\ \hline \\ C \\ \hline \\ H \\ H$			

Summary of Key Pharmacokinetic Parameters					
Linearity/non-linearity	Mean C_{max} and AUC increase less than proportionally beyond doses of 400 mg twice daily.				
Steady state	Achieved after 7 days of twice-daily dosing.				
Elimination half-life	25-48 h				
Cmax	3.32 mg/L (400 mg BID, steady state) ¹ .				
C24	No data				
AUC	28.91 mg*h/L (400 mg BID, steady state) ¹ .				
Ттах	3 h				
Bioavailability	Absolute bioavailability is unknown. The mean relative bioavailability of the tablets is 38-49%, as compared to the oral solution.				
Absorption	Absorption with a moderate-fat meal does not alter absorption.				
	Absorption with a high-fat meal decreases by 29%, as compared to fasted administration.				
Protein Binding	99.5%				
Volume of Distribution	213 L (estimated from PPK study) ² .				
CSF:Plasma ratio	No data				
Renal Clearance	19% of the dose excreted in urine as glucuronidated metabolites.				
Renal Impairment	No dosage adjustment required in mild-severe renal impairment.				
Hepatic Impairment	No dosage adjustment required in mild-moderate hepatic impairment. No data are available for patients with severe hepatic impairment (Child-Pugh C). Sorafenib exposure may be increased in these patients.				
Metabolism and Distribution					
Metabolised by	CYP3A4, UGT1A9.				
Inducer of	None expected.				

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Inhibitor of P-gp, UGT1A9, UGT1A9 (in vitro), OATP1B1³.

Transported by OATPB1/B3 (*in vitro*)⁴.

References

Unless otherwise stated (see below), information is from: Nexavar Summary of Product Characteristics, Bayer plc, September 2019. Nexavar Prescribing Information, Bayer HealthCare, June 2020.

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- 2. Jain, L., Woo, S., Gardner, E.R., Dahut et al. 2011. Population pharmacokinetic analysis of sorafenib in patients with solid tumours. British Journal of Clinical Pharmacology 72(2):294–305.
- 3. Hu, S., Mathijssen, R.H.J., De Bruijn, P. et al. 2014. Inhibition of OATP1B1 by tyrosine kinase inhibitors: in vitro–in vivo correlations. British Journal of Cancer 110:894–898.
- 4. Zimmerman, E.I., Hu, S., Roberts, J.L. et al. 2013. Contribution of OATP1B1 and OATP1B3 to the Disposition of Sorafenib and Sorafenib-Glucuronide. Clinical Cancer Research 19(6):1458–1466.